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Solution Phase and Solid Supported Syntheses of End-Functionalized Poly(MMA) by Aldol-Type Reaction of Samarium(III) Enolate at the Chain End

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ABSTRACT: Aldol-type reactions of a samarium enolate at the propagating end of living anionic poly(MMA) with aldehydes were carried out. The enolate underwent aldol-type end-capping reaction with 3-phenylpropanal to give the corresponding samarium alkoxide at the polymer terminal. Successive treatment of the alkoxide with benzoyl chloride resulted in its benzoylation. End-capping reaction with 2-phenylpropanal also smoothly proceeded to give the poly(MMA) having the corresponding secondary alkoxide at the terminal. Its benzoylation was not successful; however, an intramolecular reaction of the terminal alkoxide with the methyl ester moiety of the penultimate MMA unit predominantly proceeded to give the corresponding poly(MMA) having a lactone moiety at its terminal. In addition, a terminal samarium enolate of a living poly(MMA), which was supported on polystyrene beads by a benzoyl ester-type linker, reacted with the aldehydes to afford the end-capped poly(MMA), which could be efficiently isolated from the beads by selective cleavage of the linker by trifluoroacetic acid treatment.

Introduction

One of the advantageous features of living polymerization is its end-capping reaction, which can afford polymers having functional groups at their terminals. Various end-capping reactions have been intensively developed, because the corresponding end-functionalized polymers show unique aggregation states[1] and the related functions.[2] Macromonomers with polymerizable terminals have been also synthesized by end-capping reactions and applied as building blocks to construction of various macromolecular architectures.[3]

We have reported living anionic polymerization of methacrylate, mediated by samarium(III) enolate.[4] The samarium enolate can be easily prepared by reduction of 2-bromoisobutyric acid ester with samarium diiodide (SmI_2) at the initiation stage. By virtue of this easy access to samarium enolate, well-defined synthesis of block copolymers and star polymers has been accomplished.[4] Furthermore, solid-supported samarium enolate can be analogously prepared from polystyrene beads supported bromoisobutyrate and has been applied to graft polymerization of methacrylates.[5] However, end-capping reaction of the terminal samarium enolate has not been studied yet.

Recently, organosamarium(III) reagents gain their importance as species for selective reactions such as Barbier-type and Reformatsky-type ones, due to their high reactivity toward carbonyl compounds.[6] Thus, it is expected that samarium enolate at living propagating end of poly(methyl methacrylate) [poly(MMA)] would readily react with carbonyl compounds to give the corresponding end-capped polymers. This article describes the reaction of the living end with aldehyde and that of the resulting samarium alkoxide. Analogous end-capping reactions of living poly(MMA) anion supported on polystyrene beads were also performed for the purpose of solid-supported synthesis of end-functionalized poly(MMA).

Results

1. End-Capping Reaction of Living Poly(MMA) Anion. Anionic polymerization of MMA was initiated by reduction of benzyl 2-bromoisobutyrate (**1**) with SmI_2 in the presence of MMA and *N*,*N*-diethylpivaloylamide (DEPA) (Scheme 1).[4] To the resulting tetrahydrofuran (THF) solution of the living polymer **2** was added 3-phenylpropanal. The yellow color corresponding to the terminal samarium(III) enolate of **2** immediately disappeared, suggesting that the enolate underwent aldol-type reaction with aldehyde efficiently. After quenching the reaction by dilute hydrochloric acid, the corresponding polymer **4a** was obtained in a high yield (81%, entry 1 in Table 1). SEC analysis of the polymer showed a unimodal and narrow peak. ^{1}H NMR analysis of the obtained polymer revealed that a benzyl group was incorporated into the polymer, indicating that the polymerization was successfully initiated by samarium(III) enolate derived from **1** (Figure 1a). In addition, the spectrum exhibited a signal attributable to a methine proton of a secondary hydroxyl group, which was arisen by the reaction of the living poly(MMA) with the aldehyde. Using the signal corresponding to the benzylic protons at the initiation end as a standard, relative intensities of the signals corresponding to the terminal structure were calculated. The calculated value supported the excellent end-capping efficiency. Thus, the samarium enolate at the chain end of the polymer is highly reactive with aldehyde, even though it is sterically much more hindered than low molecular weight enolates. Successful formation of the alkoxide terminal

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Scheme 1

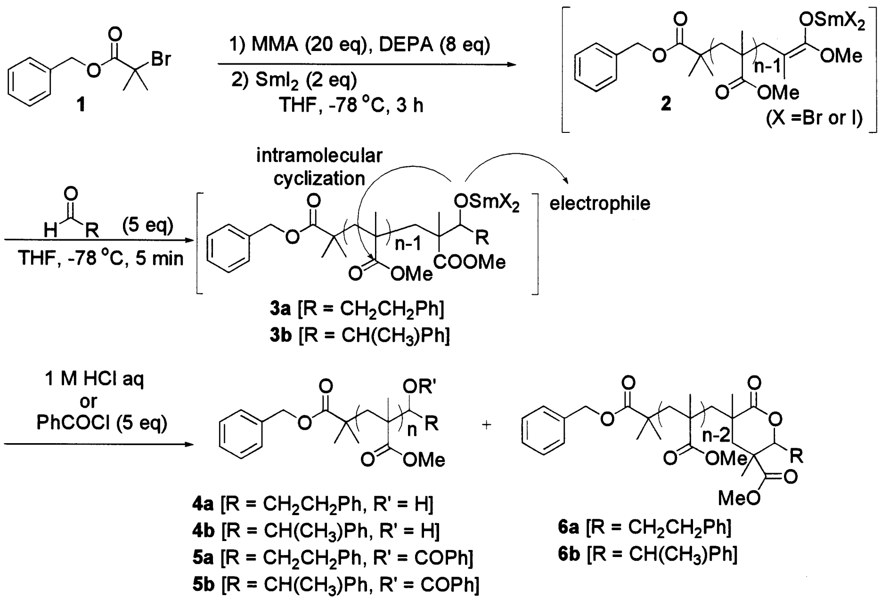
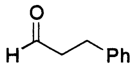
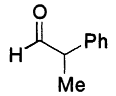


Table 1. End-Capping Reactions in Solution

Entry	End-capping with aldehyde		Quenching or 2nd stage end-capping		Obtained polymer	$M_n(M_w/M_n)$[c]
	Aldehyde	f'[a]	Electrophile	f'[a]	(Yield / %[b])	of the polymer mixture
1		> 0.95	1M HCl aq	–	**4a** (81)	4,700 (1.08)
2		> 0.95	PhCOCl[d]	> 0.95	**5a** (77)	5,000 (1.08)
3		> 0.95	1M HCl aq	–	**4b** (60)	6,600 (1.06)
4		> 0.95	PhCOCl[d]	0.67	**4b** (30) + **5b** (13) + **6b** (47)[e]	4,000 (1.10)

[a] Determined by ^{1}H NMR. [b] Hexane-insoluble parts. [c] Estimated by SEC (eluent: THF, poly(MMA) standards). [d] Conditions: 5 min at −78 °C. [e] **4b**:**5b**:**6b** = 33:15:52.

prompted us to apply it to further end-functionalization, because it will expand the structural diversity of the chain end. When the terminal samarium alkoxide (**3a**; R = CH_2CH_2Ph) was treated with benzoyl chloride (entry 2 in Table 1), it was successfully benzoylated. ^{1}H NMR analysis of the obtained polymer revealed that the signal attributable to the methine proton of the terminal secondary hydroxyl group completely disappeared, and signals attributed to the corresponding benzoyl group appeared (Figure 1b). Quantitative efficiency in the benzoylation was confirmed from the integration ratio of the signals at the aromatic region.

End-capping reaction by 2-phenylpropanal also successfully gave the corresponding polymer (**4b**) having a secondary hydroxyl group at the terminal (entry 3 in Table 1, Figure 1c). In this case, sterically bulkier secondary alkoxide **3b** is considered to be formed. Thus, its successive benzoylation was carried out similarly to that of **3a**. Figure 1d shows the expanded ^{1}H NMR spectrum of the obtained polymer mixture. Compared with Figure 1c, the intensity of the signal f (4.2 ppm) was reduced. Using the signal b, attributable to the benzylic protons at the initiating end, as a reference, conversion of the terminal alkoxide in the acylation experiment can be roughly estimated to be 70%, suggesting that the acylation of the terminal secondary alkoxide is more sterically affected than that of the primary one (Table 1, entry 2 vs 4). A new doublet signal appeared at 4.7 ppm, indicating the formation of the corresponding acylated terminal. The efficiency in acylation, calculated on the basis of comparison of the signal intensities, was 67%, which is in good accordance with the conversion. Signals attributable to benzoyl moiety were also observed; however, the corresponding integrated intensity was much weaker than that expected from the conversion. From ^{1}H NMR data, the benzoylation efficiency was calculated to be 15%. Thus, the remaining 52%, having another acylated terminal, is considered to be arisen from unexpected reaction of terminal alkoxide. Since the molecular weight distribution of the obtained polymer is quite narrow (1.09), it is assumed that the acylation occurred not in an *intermolecular* manner (polymer−polymer binding) but in an *intramolecular* manner through substitution of methyl

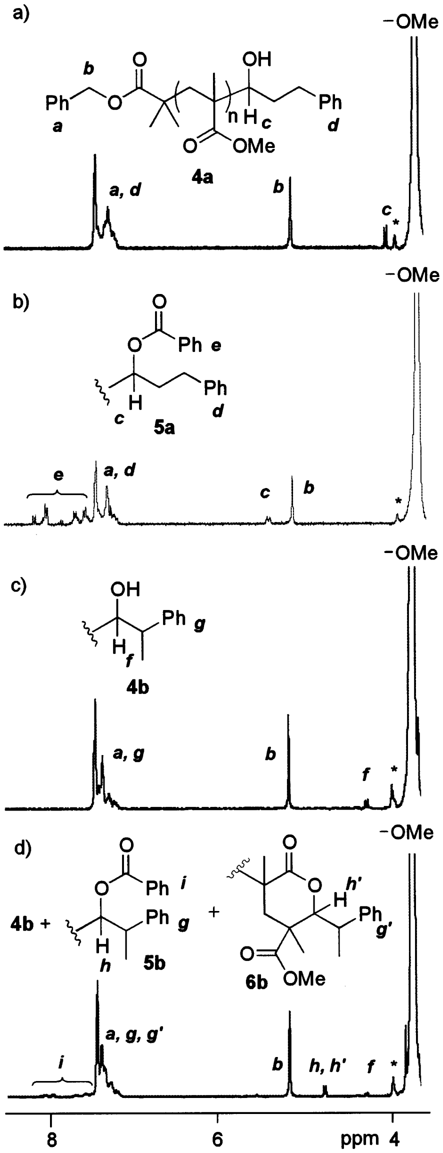


Figure 1. Expanded ^{1}H NMR spectra (300 MHz, in acetone-d_6, 3.5–8.5 ppm) of (a) **4a**, (b) **5a**, (c) **4b**, and (d) a mixture of **4b**, **5b**, and **6b**. (*) Spinning sideband.

ester of the penultimate MMA unit with the terminal samarium alkoxide. The resulting terminal structure of the polymer **6b** would be a six-membered lactone moiety. This type of intramolecular cyclization of samarium alkoxide is often involved in lactone synthesis via samarium(III)-mediated Reformatsky-type and Barbier-type reactions.[7]

2. End-Capping Reaction of Solid-Supported Living Poly(MMA) Anion. Recently, living polymerization on the cross-linked polystyrene beads has attracted much attention as a new method for well-defined synthesis of functional polymers, because the polymers formed on beads can be easily separated from residual monomers and catalysts by filtration before cleavage from the beads under appropriate conditions. Photoiniferter radical polymerization[8] and atom transfer radical polymerization[9] have been applied to the beads-supported system; however, these radical processes have limitations in end-functionalization. In contrast, our anionic process mediated by samarium enolate will be more suitable for this purpose as demonstrated by the end-capping reaction with aldehydes in a solution.

Table 2. Chemical Shifts of Methine Protons at the Chain Ends

entry	poly(MMA)	chemical shift/ppm[a]
1	**4a**	3.99
2	**4b**	4.16
3	**5a**	5.39
4	**5b**	4.67
5	**6b**	4.67
6	**13a**	4.36
7	**14a**	5.38
8	**15b**	4.67

[a] Measured by ^{1}H NMR (acetone-d_6, 300 MHz).

According to our previously reported procedure, the polymerization was initiated by reduction of 2-bromoisobutyrate moiety of **7** with SmI_2 in the presence of MMA and DEPA (Scheme 2).[5] The deep purple color based on SmI_2 turned yellow within 1 h, suggesting successful formation of beads-supported samarium(III) enolate. When 3-phenylpropanal was added to the resulting beads **8** bearing living polymer with samarium(III) enolate, the beads kept yellow color attributable to the samarium(III) enolate for a few minutes, indicating that the reaction is slower than that in solution. Such deceleration is commonly observed in beads-supported reaction, because the reaction rate largely depends on the diffusion rate of reagents into beads.[10] The reaction was quenched by aqueous hydrochloric acid, and the beads were washed with appropriate solvents in order to remove excess amount of reagents and then dried under vacuum. The obtained beads **10a** were colorless, indicating complete removal of residual reagents, and gained their weight as much as the monomer and aldehyde fed. Treatment of the beads with TFA resulted in selective cleavage of benzyl ester moiety at the initiating end to give the corresponding end-capped poly(MMA) **13a** having a narrow molecular weight distribution (entry 1 in Table 3). The successful end-capping reaction was confirmed by the ^{1}H NMR spectrum of the obtained polymer, which showed signals attributed to a methine proton of the secondary hydroxyl group at the polymer terminal (Figure 2a). It is noteworthy that the methine signal of the terminal of the polymer **13a**, having carboxyl group at the initiating end, was appeared at a lower magnetic field than that of the polymer **4a**, having benzyl ester group at the initiating end. This observation suggested the presence of hydrogen bonding between the hydroxyl and carboxyl terminals in an inter- and/or an intramolecular manner. The end-capping efficiency (f) was calculated using the ^{1}H NMR signals of the terminal structure and side chain methyl ester as follows: First, the polymerization degree (n) of the polymer was estimated by SEC based on calibration using standard poly(MMA)s. Because the theoretical number of the terminal phenyl protons and the side chain methoxy protons are 5 and $3n$, respectively, the corresponding ^{1}H NMR signals attributable to these protons would appear with intensities in the ratio of $5f$:$3n$. Thus, f can be described by the equation $f = (3n/5)x$, where x represents the observed relative intensity of the terminal phenyl protons to the side chain methoxy protons. The end-capping efficiency thus calculated was as high as >0.80.[12] Therefore, it is concluded that the samarium(III) enolate at the polymer terminal is highly reactive toward the aldehyde, even though the polymer is supported on solvent-insoluble polystyrene beads. Successive benzoylation of the terminal alkoxide **9a** was also successful as observed in the solution phase reaction (entry 2 in Table 3). The

Scheme 2

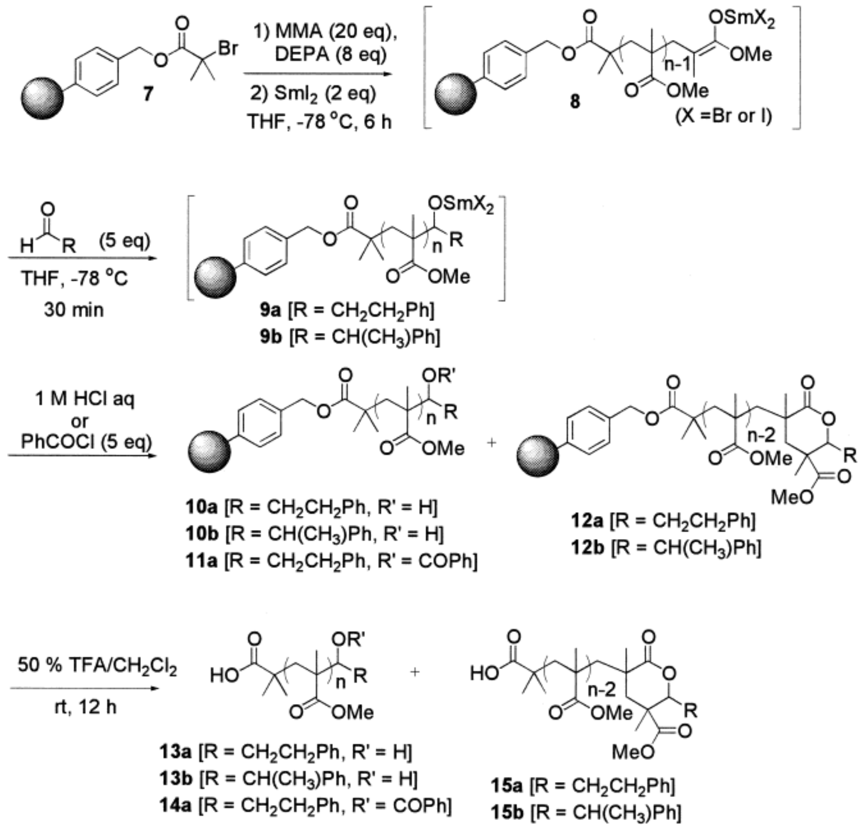
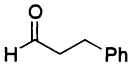
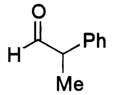


Table 3. Solid-Supported Synthesis of End-Functionalized Poly(MMA)

Entry	End-capping with aldehyde		Quenching or 2nd stage end-capping		Obtained polymer (Yield / %^{c})	*M*n(*M*w/*M*n)^d of the polymer mixture
	Aldehyde	*f*^{a}	Electrophile	*f*^{b}		
1		80	1M HCl aq	–	**13a** (93)^e	3,900 (1.08)
2		> 95	PhCOCl^f	80	**13a** (16) + **14a** (64)	3,700 (1.12)
3		> 95	1M HCl aq	–	**15b** (80)	5,000 (1.09)

[a] Calculated from integration ratio of ^{1}H NMR signals and SEC-estimated polymerization degree.[12] [b] Determined by ^{1}H NMR. [c] Hexane-insoluble parts. [d] Estimated by SEC (eluent: THF, poly(MMA) standards). [e] Obtained as a mixture with uncapped poly(MMA) derived from **8**. [f] Conditions: for 30 min at −78 °C.

obtained beads were treated with TFA to isolate the corresponding end-capped poly(MMA) having a narrow molecular weight distribution (M_w/M_n = 1.12) in 80% yield. Incorporation of benzoyl moiety was confirmed by appearance of ^{1}H NMR signals of the corresponding aromatic protons in a lower magnetic field than those of the other aromatic protons derived from the aldehyde (Figure 2b). Beside these signals, two signals were observed at 4.36 and 5.38 ppm. The former is attributed to the methine proton of the terminal hydroxyl group, and the newly appeared latter one corresponds to the methine proton of the acylated moiety, whose chemical shift agreed with that of the analogous polymer **5a** obtained by solution phase reaction. The efficiency of acylation reaction was calculated to be 80% from the integration ratio of these signals.

Next, the end-capping reaction with 2-phenylpropanal was similarly carried out (entry 3 in Table 3). The obtained beads were treated with TFA to obtain the corresponding polymer. Unexpectedly, the ^{1}H NMR signal of the terminal methine proton did not appear in the region expected for a secondary alcohol moiety but appeared at 4.7 ppm (Figure 2c), indicating the formed samarium alkoxide was already acylated before acylating reagent was added (see Figure 1d); the terminal structure of the obtained polymer **15b** is considered to be a six-membered lactone. Exclusive formation of lactone could be responsible for elongated reaction time, which would allow completion of intramolecular cyclization of the formed alkoxide. In contrast, the less bulky samarium alkoxide **9a**, formed by end-capping with 3-phenylpropanal, did not undergo such

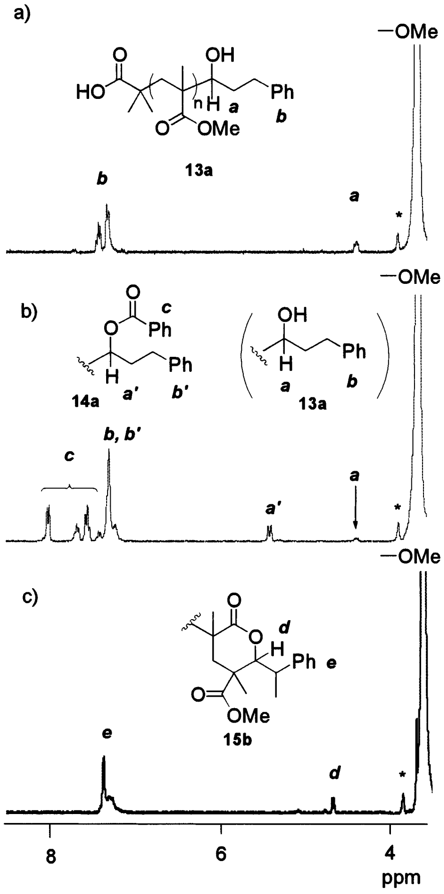


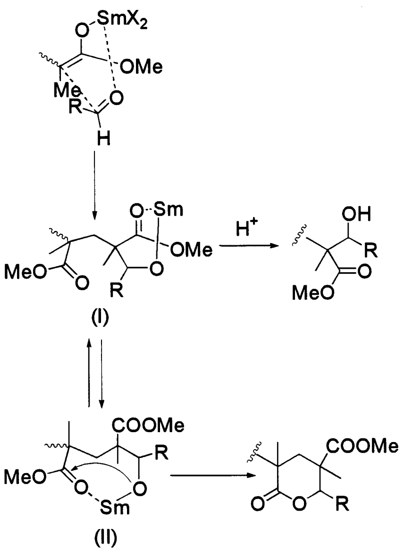
Figure 2. Expanded ^{1}H NMR spectra (300 MHz, in acetone-d_6, 3.5−8.5 ppm) of (a) **13a**, (b) a mixture of **13a** and **14a**, and (c) **15b**. (*) Spinning sideband.

intramolecular cyclization even though the reaction time was prolonged (2 h) and the temperature was elevated to room temperature.

Discussion

As can be seen from the results, the terminal samarium enolate efficiently reacted with aldehydes to afford the corresponding terminal samarium alkoxide. The terminal "secondary" alkoxide, formed by the reaction of terminal samarium enolate with 2-phenylpropanal, strongly tended to undergo intramolecular cyclization, both in the solution phase reaction and in the solid-supported one. On the other hand, the "primary" alkoxide did not undergo cyclization at all, even after 2 h at room temperature, while it can be smoothly acylated by benzoyl chloride at −78 °C. Thus, there are exactly opposite two effects of the bulkiness of the terminal alkoxide, i.e., (1) interfering with undergoing intermolecular acylation and (2) promoting intramolecular acylation (lactonization). The mechanism for the latter is not clear at present; however, it is correlated with stability of the six-membered ring formed by aldol-type reaction, which is kept by coordination of the samarium atom to the neighboring carbonyl group (Scheme 3). The presence of a bulky substituent R is unfavorable to maintain the six-membered ring (I) and promotes intramolecular ligand exchange to form an eight-membered ring (II) involving coordination of oxygen of the penultimate MMA unit, which is much more free from steric repulsion between the substituents. Thus, samarium alkoxide in II attacks the side chain methyl ester to form a thermodynamically favorable six-membered lactone at the terminal.

Scheme 3



Summary

Samarium(III) enolate at the living poly(MMA) terminal reacted with aldehydes to afford the corresponding polymers having samarium alkoxide at the terminals. The primary alkoxide, formed by end-capping with a primary aliphatic aldehyde, readily acylated with benzoyl chloride to afford the corresponding poly(MMA) having ester moiety at the terminal. In contrast, the sterically more hindered secondary alkoxide, formed by end-capping with a secondary aliphatic aldehyde, attacked the methyl ester moiety of the penultimate MMA unit to afford a six-membered lactone at the terminal. These reactions were also successfully performed on solid support using living poly(MMA) immobilized on polystyrene beads, demonstrating the feasibility of our idea about application of the present samarium(III) enolate-mediated anionic polymerization to construction of a library of polymeric materials with various terminal structures.

Experimental Section

Materials. THF was dried over sodium benzophenone under nitrogen and was distilled prior to use. MMA and DEPA were dried over CaH_2 and distilled under reduced pressure. 2-Phenylpropanal and 3-phenylpropanal were dried over $CaSO_4$ and distilled under reduced pressure. Benzoyl chloride were dried over $CaCl_2$ and distilled under reduced pressure. Hydroxymethylated cross-linked polystyrene (substitution: 0.87 mmol/g, 100−200 mesh) was purchased from Nova Biochem. A THF solution of SmI_2 was prepared according to the reported procedure.[11]

Instruments. The 300 MHz ^{1}H NMR spectra were recorded with a JEOL Lambda-300 spectrometer with tetramethylsilane as an internal standard. IR spectra were recorded with a Perkin-Elmer Spectrum-One, and the values are given in cm^{-1}. Number- and weight-average molecular weights (M_n and M_w) were estimated by size exclusion chromatography (SEC) on a Tosoh HLC-8120 (column: TSK gel G4000 and G2500H; eluent: THF, 1.0 mL/min, at 40 °C) equipped with RI and UV detectors, calibrated by poly(MMA) standards.

Synthesis of End-Capped Poly(MMA) with Aldehyde. *Typical procedure*: To a solution of benzyl 2-bromoisobutyrate **1** (26.0 mg, 0.1 mmol) in THF (1 mL), MMA (187 mg, 2.00 mmol) and DEPA (126 mg, 0.801 mmol) were added under N_2.

After cooling the mixture to −78 °C, SmI_2 (0.1 M solution in THF, 2 mL; 0.2 mmol) was added to the mixture, and the resulting mixture was stirred at −78 °C. After 3 h, 3-phenylpropanal (67.3 mg, 0.50 mmol) was added to the mixture at −78 °C, and the mixture was stirred at the temperature for 5 min. To the resulting solution, 1 M hydrochloric acid was added, and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Precipitation of the resulting mixture with hexane gave the end-capped poly(MMA) **4a** (174 mg, 87% yield) as a white powder.

Solid-Supported Synthesis of End-Capped Poly(MMA). *Typical procedure*: To a suspension of beads **7** (151 mg, bromoisobutyrate unit: 0.1 mmol) in THF (1 mL), MMA (187 mg, 2.00 mmol) and DEPA (126 mg, 0.801 mmol) were added under N_2. After cooling the mixture to −78 °C, SmI_2 (0.1 M solution in THF, 2 mL; 0.2 mmol) was added to the mixture, and the resulting mixture was shaken at −78 °C. After 6 h, 3-phenylpropanal (67.3 mg, 0.50 mmol) was added to the mixture at −78 °C, and the mixture was shaken at the temperature for 30 min. To the resulting mixture, 1 M hydrochloric acid (5 mL) was added. The beads were filtered, washed successively with water, THF, and methanol, and were dried under vacuum to obtain the beads bearing end-capped poly(MMA) **10a** (299 mg; quantitative).

In the case of sequential end-capping with 3-phenylpropanal and benzoyl chloride on the solid support, benzoyl chloride (70.3 mg, 0.50 mmol) was added at −78 °C instead of hydrochloric acid, and the mixture was shaken at the temperature for 30 min. The beads were filtered, washed successively with water, THF, and methanol, and dried under vacuum to obtain the beads bearing end-capped poly(MMA) **11a** (310 mg; quantitative). The beads **11a** (100 mg, bearing 62 mg of end-capped poly(MMA)) were swelled in 2 mL of TFA and 2 mL of CH_2Cl_2 and shaken at room temperature for 12 h. The mixture was filtrated, and the residual beads were washed with CH_2Cl_2. The filtrates were and concentrated under reduced pressure to give the end-capped poly(MMA) **14a** (62 mg; quantitative) as a white powder.

References and Notes

(1) (a) Apperloo, J. J.; Janssen, R. A. J.; Malenfant, P. R. L.; Fréchet, J. M. *Macromolecules* **2000**, *33*, 7038. (b) Folmer, B. J. B.; Sijbesma, R. P.; Versteengen, R. M.; van der Riji, J. A. J.; Meijer, E. W. *Adv. Mater.* **2000**, *12*, 874.

(2) (a) Kataoka, K.; Harada, A.; Wakebayashi, D.; Nagasaki, Y. *Macromolecules* **1999**, *32*, 6892. (b) Lee, W.-K.; Losito, I.; Gardella, J. A., Jr.; Hicks, W. L., Jr. *Macromolecules* **2001**, *34*, 3000.

(3) (a) Hayashi, M.; Nakahama, S.; Hirao, A. *Macromolecules* **1999**, *32*, 1325. (b) David, G.; Alupei, V.; Simionescu, B. C. *Eur. Polym. J.* **2001**, *37*, 1353.

(4) (a) Narita, M.; Nomura, R.; Endo, T. *Macromolecules* **1998**, *31*, 2774. (b) Narita, M.; Nomura, R.; Tomita, I.; Endo, T. *Macromolecules* **2000**, *33*, 4979.

(5) Tanaka, M.; Sudo, A.; Sanda, F.; Endo, T. *Chem. Commun.* **2000**, 2503.

(6) For recent examples: (a) Lu, L.; Chang, H.-Y.; Fang, J.-M. *J. Org. Chem.* **1999**, *64*, 843. (b) Wang, W.; Xu, M.-H.; Lei, X.-S.; Lin, G.-Q. *Org. Lett.* **2000**, *2*, 3773. (c) Nodono, M.; Tokimitsu, T.; Tone, S.; Makino, T. *Macromol. Chem. Phys.* **2000**, *201*, 2282. (d) Farcas, S.; Namy, J.-L. *Tetrahedron* **2001**, *57*, 4881. (e) Aurrecoechea, J. M.; Perez, E.; Solay, M. *J. Org. Chem.* **2001**, *66*, 564.

(7) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.

(8) Otsu, T.; Yamashita, K.; Tsuda, K. *Macromolecules* **1986**, *19*, 287.

(9) Angot, S.; Ayres, N.; Bon, S. A. F.; Haddleton, D. M. *Macromolecules* **2001**, *34*, 768.

(10) Vanio, A. R.; Janda, K. D. *J. Comb. Chem.* **2000**, *2*, 579.

(11) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

(12) Since this calculation method is based on ^{1}H NMR and SEC analysis, the calculated value would have significant errors. Thus, the conversion of the enolate to alkoxide appeared to be 80% in entry 1 while >95% in entry 2.

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