

Syntheses of Poly(ethylene oxide) Macromonomers Carrying Tertiary Amine and Quaternary Ammonium End Groups

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(Received January 23, 2003; Accepted March 30, 2003)

ABSTRACT: *p*-Vinylbenzyl alcohol, partially alkoxided with potassium naphthalene, was used successfully to initiate living polymerization of ethylene oxide to afford α -*p*-vinylbenzyl- ω -hydroxy poly(ethylene oxide) (PEO) macromonomers. The ω -hydroxy end-groups were quantitatively transformed to tertiary amines either by tosylation followed by reaction with potassium 2-dimethylaminoethoxide or by Williamson synthesis with 2-dimethylaminoethyl chloride in the presence of sodium hydride. ω -Quaternary ammonium-ended PEO macromonomers were also quantitatively obtained by reaction with iodomethane.

KEY WORDS Poly(ethylene oxide) / Macromonomers / *p*-Vinylbenzyl End-Group / Tertiary Amine End-Group / Quaternary Ammonium End-Group / End-Group Transformation / Hetero-telechelics /

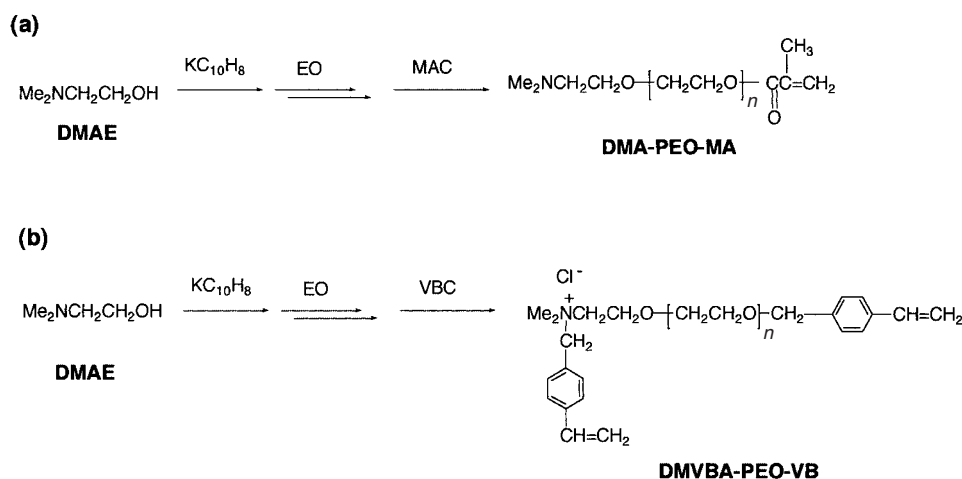
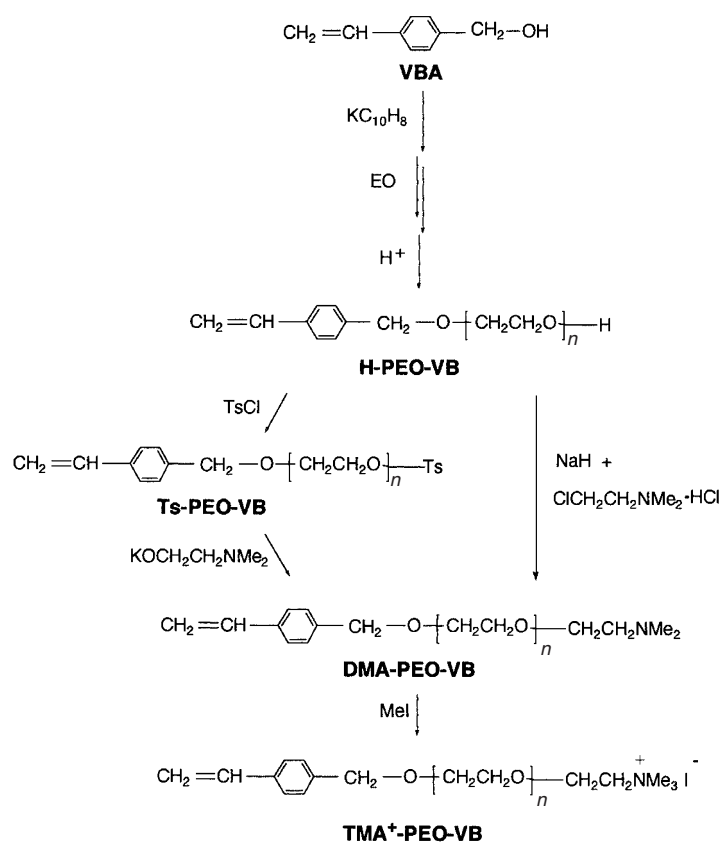
Poly(ethylene oxide) (PEO) is one of well-known, water-soluble, nonionic polymers, and its macromonomers have also been a subject of considerable interest because of their unique amphiphilic properties as well as their many potential applications in various fields, including coatings, cosmetics, ion-conductors, polymeric catalysts, and reagents, and biomedical.¹ As usual, styryl or methacryloyl functions have been introduced as a (co)polymerizable end group, say α -end group, of the macromonomer, while the other ω -end group is also feasible to introduce another functionality. So far to our knowledge, hydroxyl,^{2,3} carboxylate,^{4–6} sulfonate,^{7,8} aldehyde,^{9,10} and perfluoroalkyl¹¹ groups have been reported. In most cases^{3–11} some elaborate procedures have been involved either in anionic polymerization of ethylene oxide (EO) or in end-group transformation, while 2-hydroxyethyl methacrylate was used together with a Lewis acid to initiate cationic EO polymerization to give poly(ethylene glycol) monomethacrylate in one step.²

Our recent strategy in PEO macromonomer synthesis includes initiation of anionic EO polymerization with a functional alcohol, F–OH, as suggested by the original work by Rempp *et al.*, who used potassium *p*-isopropenylbenzylate to have a corresponding macromonomer.¹² Very recently Soula and Guyot⁷ used potassium *p*-vinylbenzylate to sequentially polymerize butylene oxide and EO to a block macromonomer with a sulfonate end group. In our methodology, a functional alcohol was partially alkoxided with potassium naphthalene (KC₁₀H₈) in tetrahydrofuran (THF) to polymerize EO in a living fash-

ion to afford F– and –OH end-functionalized PEO, F–O[CH₂CH₂O]_{*n*}–H, after acidification. In fact, we could readily have α -*p*-vinylphenylalkyl- ω -hydroxy-ended PEO macromonomers in one step.¹³ On the other hand, the ω -hydroxy-end may be transformed to introduce another functionality, F', to F–O[CH₂CH₂O]_{*n*}–F'. Thus the strategy can be of potential use in syntheses of various hetero-telechelic PEOs in general. In fact, we have used 2-dimethylaminoethanol (DMAE) K-alkoxide as an initiator of EO polymerization followed by reaction with methacryloyl chloride (MAC) to afford 2-dimethylaminoethoxy-ended PEO-methacrylate macromonomer (Scheme 1a).¹⁴ Similarly the partial alkoxide of 3-thiophenyl ethanol afforded 3-thiophene-ended PEO methacrylate¹⁵ which can polymerize *via* either oxidative (FeCl₃) or radical polymerization.

In this paper, we discuss a general process to prepare α -*p*-vinylbenzyl-ether and ω -tertiary amine-ended PEO macromonomers and their quaternization to have positively charged ends, interesting as the counterparts of those carrying the carboxylate or sulfonate end groups.^{4–8} The charges introduced are expected to add stability to the polymeric microspheres and to prepare extended PEO brushes. Therefore we first tried polymerization of EO with DMAE alkoxide followed by reaction with *p*-vinylbenzyl chloride (VBC). The product obtained, however, was found to include quaternization of the initiator fragment by VBC in addition to the expected *p*-vinylbenzyl ether end-group (Scheme 1b). So instead, we started with *p*-vinylbenzyl alcohol to initiate polymerization of EO, followed by end-group functionalization to introduce tertiary amino groups (Scheme 2).

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**Scheme 1.****Scheme 2.****EXPERIMENTAL***Materials*

p-Vinylbenzyl alcohol (VBA) was prepared from VBC by reaction with sodium acetate followed by alkaline hydrolysis, according to the procedure described,⁷ and distilled over calcium hydride (CaH₂) under high-vacuum line, and sealed into calibrated tubes with a breakable seal. Commercial 2-dimethylaminoethyl chloride hydrochloride (DMAC-HCl) (Aldrich) was dried by evacuation under vacuum. 2-

Dimethylaminoethanol (DMAE) (Tokyo Kasei Kogyo) was distilled over CaH₂ under vacuum. Commercial sodium hydride (NaH) dispersion (60% in oil) (Kishida Chemical), iodomethane (MeI) (Tokyo Kasei Kogyo), and *p*-toluenesulfonyl chloride (TsCl) (Kanto Kagaku) were used as supplied.

Tetrahydrofuran (THF) was distilled from a blue solution with sodium benzophenone. For vacuum line experiment, it was further dried and purified by distillation over LiAlH₄ and then over sodium anthracene, and finally from a red solution with disodium salt of α -methylstyrene tetramer (Na₂MS₄) into calibrated

flasks with a breakable seal. A solution of Na_2MS_4 in THF was prepared by reaction of α -methylstyrene with sodium mirror at room temperature, filtered, and stocked as dilute solutions in ampoules with a breakable seal. EO was distilled trap-to-trap twice over KOH pellets, three times over CaH_2 powder, and finally over Na mirror into calibrated tubes with a breakable seal.

Potassium naphthalene (KC_{10}H_8) was prepared under high vacuum by reacting naphthalene with excess potassium mirror in THF. Naphthalene was purified by sublimation and dissolved in THF. Potassium mirror was prepared on the wall of a flask after careful trap-to-trap distillations over a small oxygen-free flame. The dark green solution obtained was filtered and divided into calibrated tubes with a breakable seal. The concentration was usually 0.2–0.5 N, as determined by titration of an aliquot in water with a potassium hydrogen phthalate solution.

Polymerization of EO

Polymerization was conducted under high vacuum (5×10^{-5} Torr or 3.7×10^{-3} Pa) with all the reagents sealed into appropriate, calibrated ampoules which were also prepared under the vacuum with breakable seal technique.^{13–15} Ampoules including a washing solution (Na_2MS_4 in THF), VBA as an initiator, THF as a solvent, potassium naphthalene solution ($\text{KC}_{10}\text{H}_8/\text{THF}$), and EO were respectively attached into a polymerization flask with a magnetic bar (Figure 1). The apparatus was attached to a vacuum line, evacuated, baked over an oxygen-free flame, and sealed off from the line. The breakable seal of the ampoule of the washing solution (a) was broken with a magnetic bar to rinse all the inner walls. The walls were then completely washed and cleaned by fresh THF, which

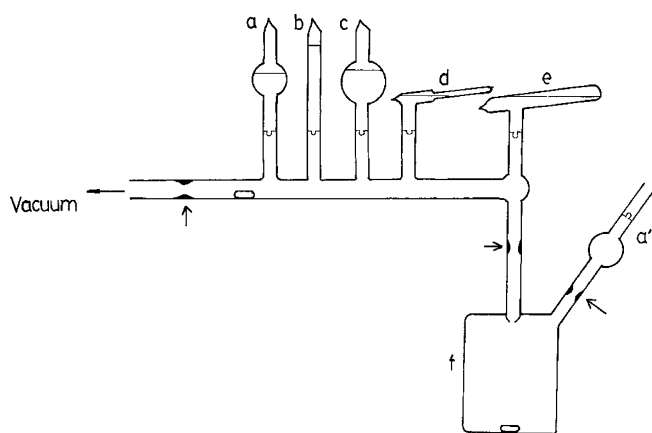


Figure 1. Apparatus for EO polymerization. a, Washing solution ($\text{Na}_2\text{MS}_4/\text{THF}$); a', ampoule for recovering a washing solution; b, potassium naphthalene solution ($\text{KC}_{10}\text{H}_8/\text{THF}$); c, THF; d, initiator alcohol (VBA); e, EO; f, reaction flask. Arrows at the thick wall indicate the points of sealing off.

comes on distillation by cooling on the outer walls with cotton tips wetted with isopropanol chilled by dry ice, until the red color of the Na_2MS_4 disappeared from the wall. The washing solution was recovered into the flask (a') and sealed off. VBA (d) and solvent (THF) (c) were introduced into the reaction flask. Then the $\text{KC}_{10}\text{H}_8/\text{THF}$ solution (b) was introduced drop by drop into the flask under vigorous magnetic stirring, so that the dark green color immediately disappeared upon mixing, indicating the reaction of the alcohol to the alkoxide. The degree of alkoxylation was 40–45% in order to avoid reaction of KC_{10}H_8 with styrenic double bond.¹³ The flask was sealed off and the breakable seal of the chilled ampoule of EO (e) was finally broken to put the monomer into the reaction flask. The flask was then placed in a bath of 40°C to start the polymerization. After polymerization for a week, the content was terminated with a small amount of methanol and poured into a large amount of hexane to precipitate out the polymers (H-PEO-VB). The polymers were collected by filtration or by decantation, washed with hexane, reprecipitated three times from benzene into hexane, and finally freeze-dried from benzene.

End-Group Transformation of ω -Hydroxy-PEO Macromonomers

(1) Tosylation followed by reaction with $\text{KOCH}_2\text{CH}_2\text{NMe}_2$. A solution of H-PEO-VB in THF (10 wt vol⁻¹%) was stirred with NaOH (ca. 10 eq) for 30 min at room temperature. To this mixture, TsCl (ca. 5 eq) was dropped in over 30 min and stirred over night. The content was centrifuged and the supernatant was poured into hexane. The precipitates were dissolved in THF and reprecipitated into acetone. The salts were filtered and the filtrate was concentrated and poured into hexane. The polymers, Ts-PEO-VB, were collected, purified three times by reprecipitation, and freeze-dried from benzene under vacuum in an ampoule with a breakable seal. The ampoule was attached to a flask together with ampoules containing a washing solution, THF, and 10% excess of potassium 2-dimethylaminoethoxide in THF which had been prepared from DMAE and KC_{10}H_8 . The reaction was conducted for 24 h at room temperature under vacuum in a similar procedure as described for EO polymerization. The content was poured into acetone to salt out. The salts were filtered and the filtrate was concentrated and poured into hexane. The polymers, DMA-PEO-VB, were collected, purified similarly, and freeze-dried from benzene. The polymers were obtained in almost quantitative yield.

(2) Williamson reaction with $\text{ClCH}_2\text{CH}_2\text{NMe}_2$. A solution of H-PEO-VB in dry THF (10 wt vol⁻¹%) was

Table I. Polymerization of EO to H-PEO-VB^a

Code	VBA	KC ₁₀ H ₈	EO	H-PEO-VB			
	mmol	mmol	mmol	<i>n</i> (calc) ^b	<i>n</i> (¹ H NMR) ^c	<i>n</i> (SEC) ^d	<i>M_w/M_n</i> (SEC) ^d
H-1	24.4	9.8	385	16	21	18	1.09
H-2	14.2	5.7	578	41	46	40	1.06
H-3	10.4	4.3	290	28	29	–	–
H-4	10.4	4.7	587	57	57	–	–
H-5	5.1	2.1	552	108	106	–	–

^aTHF: *ca.* 100 mL, degree of alkoxidation: [KC₁₀H₈]/[VBA] = 0.40–0.45, temp.: 40 °C, polymerization time: 7 d, conversion: nearly quantitative. ^b*n* = [EO]/[VBA] with 100% conversion assumed. ^c*n* = (*I*_{EO}/4) / (*I*_{VBA}/2), where *I*_{EO} = peak intensity of the oxyethylene protons at δ3.7 and *I*_{VB} = peak intensity of the benzylic methylene protons at δ4.55. ^dDetermined by SEC calibrated with standard poly(ethylene glycol)s and *n* = *M_n*/44.

reacted with DMAC-HCl (5 eq) in the presence of NaH (10 eq), which had been freed from oil by washing with hexane and dried. The mixture was stirred magnetically for 2 d at 40 °C. The salts were filtered, and the filtrate was concentrated and poured into hexane. The polymers obtained, DMA-PEO-VB, were collected, three times purified by reprecipitation, and freeze-dried from benzene. The polymers were obtained in almost quantitative yield.

(3) Quaternization with MeI. DMA-PEO-VB was dissolved in dry THF (10 wt vol⁻¹%) and reacted with MeI (*ca.* 10 eq) under stirring for one d at room temperature. The content was centrifuged and the supernatant was concentrated and poured into hexane. Precipitated polymers were collected, three times purified by reprecipitation, and freeze-dried from benzene. The polymers, TMA⁺-PEO-VB, were obtained in almost quantitative yield.

Characterization

Proton nuclear magnetic resonance (¹H NMR) spectra were measured on Mercury Varian 300 with deuterio-chloroform (CDCl₃) solutions, with tetramethylsilane as an internal standard. Pulse delay time was 1.5 sec and 16 accumulations were performed. Size exclusion chromatography (SEC) was recorded on JASCO PU980 as a pump, with JASCO RI980 as an RI detector, and Shodex GPC KF-802 and -803 as columns. The eluent was THF with the flow rate of 1 mL min⁻¹ at 40 °C. The standard poly(ethylene glycol)s were used for calibration of the molecular weights.

RESULTS AND DISCUSSION

Polymerization of EO with Partially Alkoxidated VBA

In macromonomer synthesis,¹⁶ the initiation method for introducing a polymerizable end-group is of great advantage over the termination method, since the latter usually requires an excess amount of the corresponding

terminator to achieve a satisfactory functionality. On the other hand, the requirement of the former is that no reaction occurs between the propagating chain ends and the initiator fragments. As the oxy anions are believed to hardly react with styrenic double bonds, VBA was partially alkoxidated with KC₁₀H₈ to initiate polymerization of EO. Another advantage is the hydroxy group introduced as the other chain end, which may be readily transformed to different functionalities. Here for the purpose of transformation to tertiary amine and quaternary ammonium, we have prepared *α-p*-vinylbenzyl-*ω*-hydroxy-PEO macromonomers, H-PEO-VB, with various degree of polymerization, *n*, with the result given in Table I. Typical ¹H NMR spectra are given in Figures 2a and 3a.

The values of *n* calculated kinetically from the EO/VBA molar ratio, those determined by ¹H NMR, and those by SEC are in satisfactory agreement with each other. The SEC peaks are sharp in every case with narrow distribution in *n* or in molecular weight, *M_w/M_n* ≤ 1.1, as can be also seen in the SEC data in Table IV for the final products after quaternization. Therefore we can conclude again¹³ that the present polymerization proceeds in clean living mechanism with very fast equilibrium among the potassium alkoxides and the corresponding free alcohols as the active chain ends.

End-Group Transformation of *ω*-Hydroxy-PEO Macromonomers

In the first approach, the *ω*-hydroxy group was tosylated to transform into an electrophilic carbon¹⁷ and then reacted with potassium 2-dimethylaminoethoxide as a nucleophile. The results, given in Table II with the ¹H NMR in Figures 2b and 2c, are satisfactory in introducing the tosyl and the tertiary amino end groups.

The second approach is direct Williamson synthesis by reaction of the *ω*-hydroxy group with 2-dimethylaminoethyl chloride in the presence of excess NaH. The results are given in Table III with a typical ¹H NMR spectrum in Figure 3b. The end-group trans-

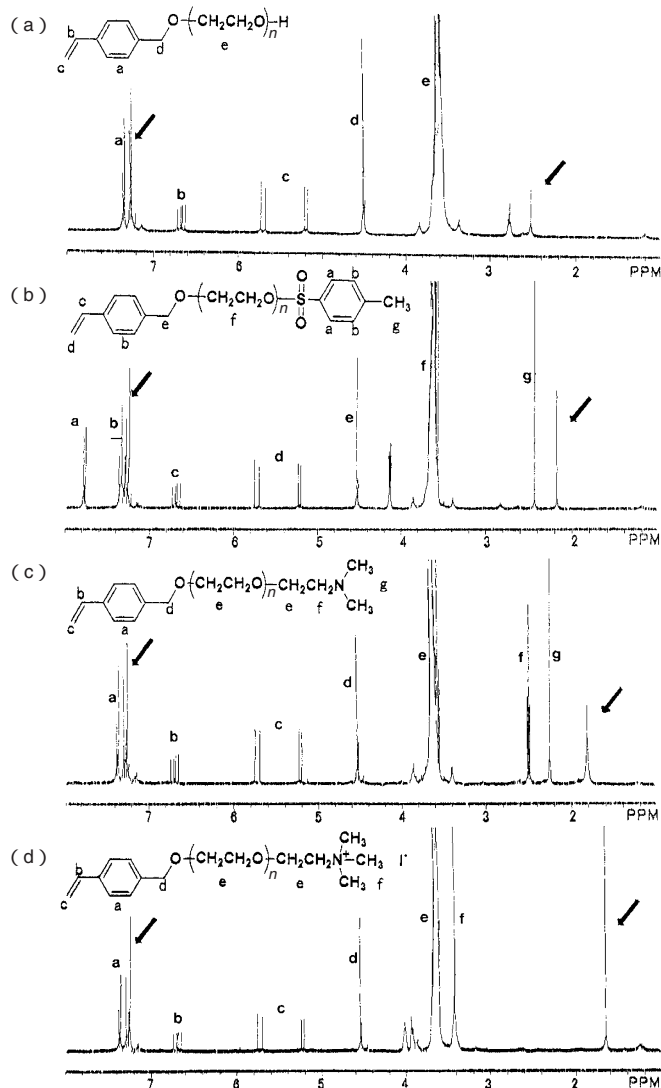


Figure 2. ¹H NMR spectra of (a) H-PEO-VB (H-1), (b) Ts-PEO-VB (Ts-1), (c) DMA-PEO-VB (N-1), and (d) DMA⁺-PEO-VB (N⁺-1). Arrows indicate impurities due to CHCl₃ and H₂O.

formation was again quantitative.

The final transformation to quaternary ammonium end-group was performed by reaction with iodomethane. The results, summarized in Table IV with typical ¹H NMR spectra in Figures 2d and 3c, again show satisfactory conversion to the quaternary ammonium end-groups. Some deviation of *n* by SEC from that by ¹H NMR may result from the calibration based on standard poly(ethylene glycol)s without the functional groups such as *p*-vinylbenzyl or trimethylammonium. We believe the ¹H NMR data are most reliable since both the values of *n* and *f* change very little through various transformations.

To summarize, throughout all the transformations performed, the end-group functionalities remain almost perfect and the polymers were isolated almost quantitatively, while the degree of polymerization, *n*, and its distribution are kept essentially the same as

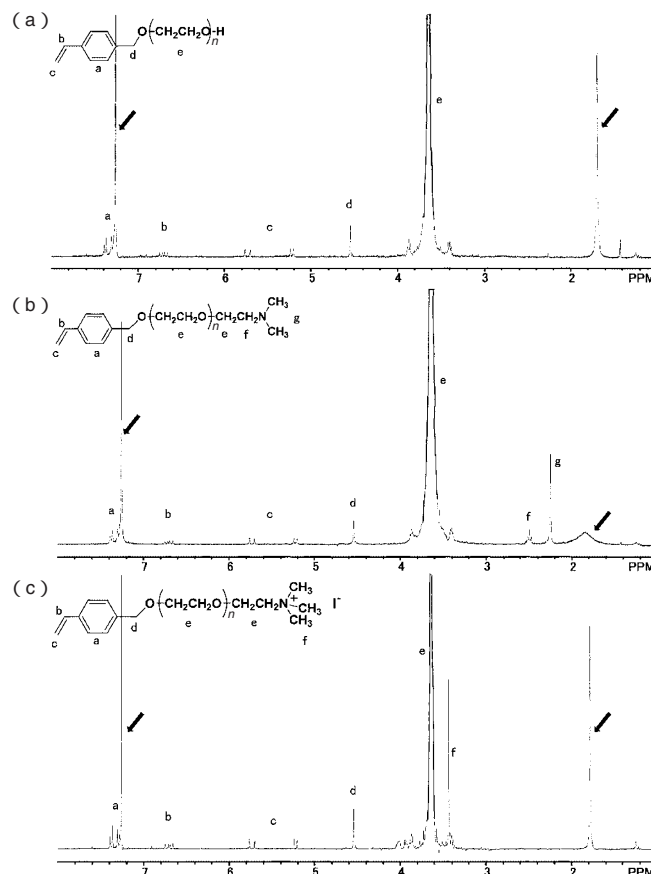


Figure 3. ¹H NMR spectra of (a) H-PEO-VB (H-5), (b) DMA-PEO-VB (N-5), and (c) DMA⁺-PEO-VB (N⁺-5). Arrows indicate impurities due to CHCl₃ and H₂O.

the original. These results suggest that the present method provides an efficient approach to functional PEO macromonomers as well as hetero-functional or hetero-telechelic PEOs in general.

CONCLUSION

Initiation of EO polymerization with partially K-alkoxidated VBA afforded well-defined α -*p*-vinylbenzyl- ω -hydroxy PEO macromonomers. ω -Hydroxy group was successfully transformed into tertiary amine either by tosylation followed by reaction with KOCH₂CH₂NMe₂ or by Williamson synthesis with ClCH₂CH₂NMe₂. Although the latter is preferred for the present objective because of simplicity, both procedures will be useful because various other kinds of nucleophiles and electrophiles may be used for desired end-group transformation. Tertiary amine groups were easily reacted with MeI to afford quaternary ammonium-ended PEO macromonomers. Application of these macromonomers to emulsion and dispersion polymerization of styrene is expected to afford monodisperse polymeric microspheres with surface functionalities such as hydroxyl and

Table II. Preparation of DMA-PEO-VB *via* Ts-PEO-VB

(a) Tosylation					
Code	H-PEO-VB	NaOH	TsCl	Ts-PEO-VB	
	code / mmol			mmol	n ($^1\text{H NMR}$) ^a
Ts-1	H-1 / 9.3	75	26	21	1.02
Ts-2	H-2 / 5.7	125	26	45	1.01
(b) Reaction with KOCH ₂ CH ₂ NMe ₂					
Code	Ts-PEO-VB	KOCH ₂ CH ₂ NMe ₂	DMA-PEO-VB		
	code / mmol		mmol	n ($^1\text{H NMR}$) ^a	f ($^1\text{H NMR}$) ^c
N-1	Ts-1 / 4.9	5.5	20	0.99	
N-2	Ts-2 / 4.2	5.8	47	0.97	

^aSee the footnote ^c in Table I. ^bFunctionality of Ts end-group: $f = (I_{\text{Me}}/3)/(I_{\text{VB}}/2)$, where I_{Me} = peak intensity of the Ts methyl group at $\delta 2.5$ and I_{VB} = peak intensity of the benzylic methylene protons at $\delta 4.55$. ^cFunctionality of Me₂N-end group: $f = (I_{\text{Me}}/6)/(I_{\text{VB}}/2)$, where I_{Me} = peak intensity of the Me₂N-methyl group at $\delta 2.3$ and I_{VB} = peak intensity of the benzylic methylene protons at $\delta 4.55$.

Table III. Preparation of DMA-PEO-VB *via* Williamson Synthesis^a

Code	H-PEO-VB	NaH	ClCH ₂ CH ₂ NMe ₂ HCl	DMA-PEO-VB	
	code / mmol			mmol	n ($^1\text{H NMR}$) ^a
N-3	H-3 / 10.4	106	60	28	1.04
N-4	H-4 / 10.4	105	56	55	1.01
N-5	H-5 / 5.1	106	59	107	0.99

^aSee the footnote ^c in Table I. ^bFunctionality of Me₂N-endgroup: $f = (I_{\text{Me}}/6)/(I_{\text{VB}}/2)$, where I_{Me} = peak intensity of the Me₂N-methyl group at $\delta 2.3$ and I_{VB} = peak intensity of the benzylic methylene protons at $\delta 4.55$.

Table IV. Preparation of TMA⁺-PEO-VB^a

Code	DMA-PEO-VB	MeI	TMA ⁺ -PEO-VB			
			n ($^1\text{H NMR}$) ^a	f ($^1\text{H NMR}$) ^b	n (SEC) ^c	M_w/M_n (SEC) ^c
N ⁺ -1	N-1 / 3.4	17	21	1.00	19	1.13
N ⁺ -2	N-2 / 1.7	8	45	0.96	40	1.08
N ⁺ -3	N-3 / 10.4	76	28	1.00	38	1.09
N ⁺ -4	N-4 / 10.4	72	55	1.01	63	1.01
N ⁺ -5	N-5 / 5.1	71	105	0.99	112	1.10

^aSee the footnote ^c in Table I. ^bFunctionality of Me₃N⁺-endgroup: $f = (I_{\text{Me}}/9)/(I_{\text{VB}}/2)$, where I_{Me} = peak intensity of the Me₃N⁺-methyl group at $\delta 3.5$ and I_{VB} = peak intensity of the benzylic methylene protons at $\delta 4.55$. ^cDetermined by SEC calibrated with standard poly(ethylene glycol)s and $n = M_n/44$.

trimethylammonium, as will be published in due course.

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