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Quantitative ω-Amination, ω-Azidolysis, and ω-Thiolation of Poly(ethylene oxide)s Through Anionic Mechanism

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Abstract: *n*-Butyllithium-initiated ring-opening polymerization of ethylene oxide with potassium *t*-butoxide in the mixture of benzene and dimethyl sulfoxide (DMSO) at 35 ºC yielded corresponding "living" polymeric alkoxide. The molecular weight was well controlled on the basis of stoichiometric balance. Quantitative chain-end functionalizations, such as the amination, the azidation, and the thiolation of polymeric alkoxide, were performed. The yields were almost quantitative (over 98 mol%). The resulting products were characterized by the combination of ^{1}H NMR spectroscopy, UV/Visible spectroscopy, FTIR, MALDI-TOF MS analysis, and size exclusion chromatographic analysis.

Keywords: poly(ethylene oxide), molecular weight control, chain-end functionalizations, amination, azidation, thiolation.

Introduction

Poly(ethylene oxide) (PEO) has been well known as a basic polymer, which is used in a variety of applications, such as a lithium-ion battery[1-5] and in the biomedical field.[6-8] Poly(ethylene glycol) (PEG) exhibits the same architecture as PEO with a relatively low molecular weight (depending on the synthetic condition) in the biomedical application field. It has been employed for a long time because it is cheap, water-soluble, and biocompatible.[9] PEG has been extensively used not only as a precursor of a PEG-conjugated pro-drug, which is chemically bonded to drug, but also a steric stabilizing moiety in polymeric micelles for the physical entrapment of active drugs in the drug delivery system.[9-12] The molecular weight, as well as the chain-end functionality of PEG/PEO, will be extremely important in affecting its properties in the physiological media.

It has been common knowledge for some time that controlled/"living" polymerization of vinyl or cyclic monomers is the best method to control both the molecular weight and the chain-end functionalities of the corresponding polymers.[13,14] Anionic ring-opening polymerizations of ethylene oxide (EO) have been performed in highly polar solvents using the initiators that have sodium or potassium alkali metal counterion.[15-18] In spite of its importance and usefulness, no simple polymerization process of EO using authentic initiators exhibiting "living" character has been reported on a commercial scale for a long time. Furthermore, no efficient and simple chain-end functionalization process of PEO has been reported. In practice, the tedious work involved in the preparation of these initiating systems under high vacuum or inert gas has limited the performance of anionic ring-opening polymerizations of EO to yield the corresponding polymers with controlled molecular weights. After significant effort, it became evident that the use of authentic initiators for the preparation of PEO seemed to overcome the limitation. For instance, alkyllithium-initiated ring-opening polymerization of EO, even in highly polar solvents or in the presence of highly basic phosphazene (P4), has been reported to provide no quantitative conversion of EO.[19] Interestingly, it has been reported that poly(styryllithium)-initiated ring-opening polymerization of EO with potassium *t*-butoxide (*t*-BuOK) in the mixture of benzene and dimethyl sulfoxide (DMSO) (7/3, v/v) yielded poly(styrene-*b*-EO) and PEO itself with a quantitative conversion of EO.[20,21] In this regard, *n*-butyllithium (*n*-BuLi)-initiated polymerization of EO in the presence of *t*-BuOK has been found to yield active polymeric alkoxide exhibiting "living" nature, which has led to the control of the molecular weight of PEO and quantitative chain-end functionalizations, such as the macromonomer or the macroinitiator.[22] In particular, it has been reported that PEO-folate conjugate obtained from the reaction of PEO-anhydride with folic acid was found to be a very efficient compound for the preparation of theranostic nanoparticles in a tumor cell.[23]

In this paper, the discussion will center around an efficient synthesis of terminally functionalized PEOs, such as ω-amine PEO, ω-azide PEO, and ω-thiol PEO *via* the chain-end tosylation process of the active polymeric alkoxide obtained from *n*-BuLi-initiated polymerization of EO in the presence

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of *t*-BuOK, and the results will be compared with those observed from the *t*-BuOK-initiated polymerization of EO.

Experimentals

Materials. Benzene (DAEJUNG Chemical Co., anhydrous, 99.8%), DMSO (DAEJUNG Chemical Co., reagent grade), and tetrahydrofuran (THF; DAEJUNG, 99%) were purified by following the modified procedures described in the literature.[20-22] EO (Lotte Chemical Co., 98%) was donated and used after the purification following the procedures as described in the literature.[20-22] Potassium *t*-butoxide (*t*-BuOK; Aldrich Chemical Co., 1.0 M solution in THF) was used as received. *n*-Butyllithium (*n*-BuLi; 1.6 M in hexane; Sigma-Aldrich Chemical Co.) was used as an initiator after titration by Gilman's method using 1,2-dibromoethane.[24] NaOH (Oriental Chemical Co., 97%), dichloromethane (DCM; Oriental Chemical Co.), and diethyl ether (DAEJUNG Chemical Co., 99.0%+) were used without further purification. Potassium thioacetate ($CH_3C(O)S^{-+}K$; Sigma-Aldrich Chemical Co., 98%) was dissolved in methanol, followed by precipitation in diethyl ether and drying in vacuum oven prior to use. Phthalimide (PTI) potassium salt (Sigma-Aldrich Chemical Co., 98.0%) and sodium azide (NaN_3; Sigma-Aldrich Chemical Co., ≥98.0%) were used as purchased. *p*-Toluenesulfonyl chloride (TsCl; Sigma-Aldrich Chemical Co., >98%) and triethylamine (Sigma-Aldrich Chemical Co., GC ≥99.5%) were also used as purchased.

Polymerization of EO. Anionic ring-opening polymerization of EO was performed in the mixture of benzene and DMSO (7/3, v/v) at 40 °C for 24 h under high vacuum. In this study, the *n*-BuLi (8.0×10^{-3} mol)-initiated ring opening process of purified EO (30 mL; *d*=0.882) was performed in 400 mL of the mixture of benzene/THF (99/1, v/v) for 6 h, followed by the addition of a *t*-BuOK solution ($[K^+]/[Li^+]$=2.0/1.0 mol/mol) and the delivery of purified DMSO (100 mL) into the reactor. The solution was left standing and was stirred at 40 °C then intermittently cooled down to 5 °C and heated up to 40 °C for further 24 h. The molecular weights of all polymers were controlled in the 2,000-10,000 g/mol range on the basis of the stoichiometric balance ([monomer(g)]/($[K^+] + [Li^+]$)(mol)). All the resulting solutions were poured into excess diethyl ether. Prior to use, the precipitate was filtered and dried in a vacuum oven at room temperature.

Synthesis of Chain-End Functionalized PEOs. All terminally functionalized PEOs were obtained *via* the reaction of "living" polymeric alkoxide with proper electrophiles, such as TsCl. Chain-end tosylation of "living" polymeric alkoxide (M_n=3,900, 3.9 g) using TsCl (0.01 mol) was carried out in the presence of trimethylamine (0.02 mol) in DCM (150 mL) at 35 °C for 24 h using a dropping funnel reactor, followed by the delivery of ammonium chloride (2 mL) then filtration and precipitation were undertaken in excess diethyl ether. The precipitate was filtered and dried in a vacuum oven for 48 h. The resulting *ω*-tosyl PEO (3.9 g) was reacted with potassium PTI (FW=185.23; 0.01 mol) in DMF (150 mL) at 90 °C for 24 h, followed by distillation of the solution using a Rotovap® evaporator and precipitation in excess diethyl ether. Deimidation of the precipitate, *ω*-PTI PEO (3.9 g), was performed using hydrazine monohydrate (0.01 mol) in ethanol (150 mL) under reflux (70 °C) for 24, followed by precipitation in excess diethyl ether. Analogously, the *ω*-tosyl PEO (M_n=3,900 g/mol; 3.9 g) was reacted with sodium azide (FW=65.01; 0.01 mol) in DMF (150 mL) at 90 °C for 24 h, followed by the distillation of a part of the solution using the Rotovap® evaporator and precipitation of the remaining solution in excess diethyl ether. The precipitate was filtered and dried in a vacuum oven at room temperature for 48 h. The resulting product, *ω*-azide PEO (3.9 g), was reduced to *ω*-amine PEO (3.8 g) using triphenyl phosphine (PPh_3; 0.01 mol) in methanol (150 mL) under refluxing (60 °C) for 24 h. The *ω*-tosyl PEO (3.9 g) was reacted with potassium thioacetate (FW=114.21; 0.01 mol) in DMF (150 mL) at 85 °C for 24 h. All products were precipitated in excess diethyl ether. *ω*-Thioacetate PEO was deacetylated in the HCl/methanol (1.0 N) solution, followed by precipitation in excess diethyl ether. The precipitate was filtered and re-dissolved in methanol, followed by precipitation in excess diethyl ether and drying in a vacuum oven at room temperature prior to analysis. The resulting *ω*-thiol PEO exhibited coupled compounds (*ca*. 60 wt%) and was reacted with triphenylphosphine (TPP) in methanol under reflux for 24 h, followed by precipitation in diethyl ether and drying.

Characterization. The size exclusion chromatography (SEC) analysis was performed at a flow rate of 1.0 mL/min in THF at 30 °C using a Water 2410 Refractometer Index Detector system equipped with a four ultra-*μ*-Styragel columns (10^5, 10^4, 10^3, and 500 Å) after calibration with standard PEO samples (Polymer Laboratories). ^{1}H NMR spectroscopic analysis was performed using a Bruker spectrometer (Model; Avance 400 (400 MHz)) in deuterated DMSO (Sigma-Aldrich Chemical Co.) or $CDCl_3$ at 25 °C. The %transmittance changes in distilled H_2O and the buffer solution were monitored using an Agilent 8453 Diode Array spectrophotometer. Thermogravimetric analysis was performed using a Shimadzu DF 50. Fourier transform infrared (FTIR) spectra were recorded on a Thermo Nicolet 380 spectrometer equipped with a smart MIRacle ATR accessory. The sample pellets used for this purpose were prepared with KBr powders. The matrix-assisted laser desorption ionization-time of flight mass spectroscopy (MALDI-TOF MS) analysis was performed using a Voyager-DE™ STR Biospectrometry Workstation (Applied Biosystems Inc.) for R-PEO-OH and an AB SCIEX TOF/TOF™ 5800 System (AB SCIEX) for *t*-BuO-PEO-OH. 2,5-Dihydroxybenzolic acid (DHB) for R-PEO-OH, and dithranol (Sigma-Aldrich: 50 mg/kg) for *t*-BuO-PEO-OH were used as the matrices for the ionization operated in the reflection mode, respectively. The matrix (10 mg) solutions were prepared using water (1.0 mL) and $CHCl_3$ (1.0 mL). The sample solution was prepared by mixing the matrix solution (1 μL) with the polymer solution

(1 μL) leading to the concentration at R-PEO-OH and *t*-BuO-PEO-OH to matrix ratio of 1:1, 1:3, 1:7, and 1:10 and dried on the 96 well plate.

Results and Discussion

Synthesis of "Living" PEOs. An efficient and simple method to obtain PEO with well-controlled molecular weight through *n*-BuLi-initiated ring-opening polymerization of EO in the presence of *t*-BuOK has already been suggested.[20,22] Concerning the "living" characteristics of polymeric alkoxide, quantitative chain-end functionalization is expected to be achieved under proper conditions. In this study, all reagents were purified under a high vacuum, and polymerizations were carried out at 35 °C under a high vacuum *via* a break-seal technique. The molecular weight of polymeric alkoxide was well controlled on the basis of the stoichiometric balance ([gram of monomer]/[*n*-BuLi+*t*-BuOK]mol). All molecular weights were controlled in the 2,000-10,000 g/mol range. *t*-BuOK as a typical anionic initiator without *n*-BuLi was also empolyed for "living" polymerization of EO. It has long been reported that, while *t*-BuOK-initiated ring opening polymerization of EO in DMSO was successfully performed,[25] methyl sulfinyl carbanion (dimsyl ion) obtained from a rapid proton transfer between *t*-BuOK and DMSO was a real initiating moiety.[26] This discussion is still in dispute. However, the acutal initiating moiety in the mixture of benzene and DMSO (7/3, v/v) seemed to consist of *n*-hexanoate and *t*-butoxide anion to initiate EO, which led to "living" polymerization. To check what the initiating moiety is, the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis is expected to provide one of the excellent tools to predit the structure of the chain end group. Figure 1 represents a typical matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) spectrum of *ω*-hydroxyl PEO (R-PEO-OH; R=*n*-$C_6H_{13}O$+*t*-BuO).

The major series of peaks corresponding to the molecular mass of R-PEO is expressed in the following eq. (1)[27]

$$m/z = \mathrm{R}\ (n\text{-}C_6H_{13}O/t\text{-BuO, mol/mol}) + n \times 44.052\ (\mathrm{EO}) + 22.99\ (Na^+) + 1\ (H^+) \quad (1)$$

In this respect, in the expanded region, one population could be observed *m*/*z*=76 (R)+*n*×44.052 (EO)+22.99 ($[Na]^+$)+1 (H^+) ($[m/z]_{exp}$=5,871.0703 *vs*. $[m/z]_{theo}$=5,870.802; *n*=131) in the case of *ω*-hydroxyl PEO. The molecular mass of *ω*-hydroxyl PEO was in excellent agreement with that calculated theoretically. In practice, based on the ^{1}H NMR spectrum of R-PEO-OH, the chain-end masses seemed to be only related with that of the *t*-butoxide group and potassium cation. Furthermore, *t*-BuOK-initiated ring-opening polymerization of EO in the mixture of benzene and DMSO (7/3, v/v) yielded an analogous product to R-PEO-OH by following the polymerization process described in the literature.[25,26] Figure 2 represents the MALDI-TOF MS spectrum of *t*-BuO-PEO-OH in the reflector mode. In the expansion region, the peak mass *m*/*z*=73 (*t*-BuO)+*n*×44.052 (EO)+39 ($[K]^+$)+1 (H^+) ($[m/z]_{exp}$=3,327.9428 *vs*. $[m/z]_{theo}$=3,328,796; *n*=73) agrees with the theoretical one in the case of *n*=73 and potassium cation. However, considering the dimsyl chain-end structure predicted from the proton abstraction of *t*-BuOK from DMSO as already mentioned in the literature,[26] the molecular mass of Dimsyl-PEO-OH is expected to be *m*/*z*=77 (Dimsyl)+*n*×44.052 (EO)+39 ($[K]^+$)+1 (H^+). In particular, irrespectively of cation, both polymerization systems produced no matched molecular masses carrying the dimsyl chain-end group. Concerning these observations, all ring-opening polymerization processes had to start by alkoxide initiation, *i.e*., no production of methyl sulfinyl carbanion (dimsyl ion) in this polymerization system. The molecular masses shown in Figure 1 and Figure 2 were well matched with the theoretical values in case of the *t*-butoxy chain end. The mechanism will be discussed in more detail through ^{1}H NMR spectral analysis. In this respect, both polymerization systems seem to have a "living" polymerization nature.

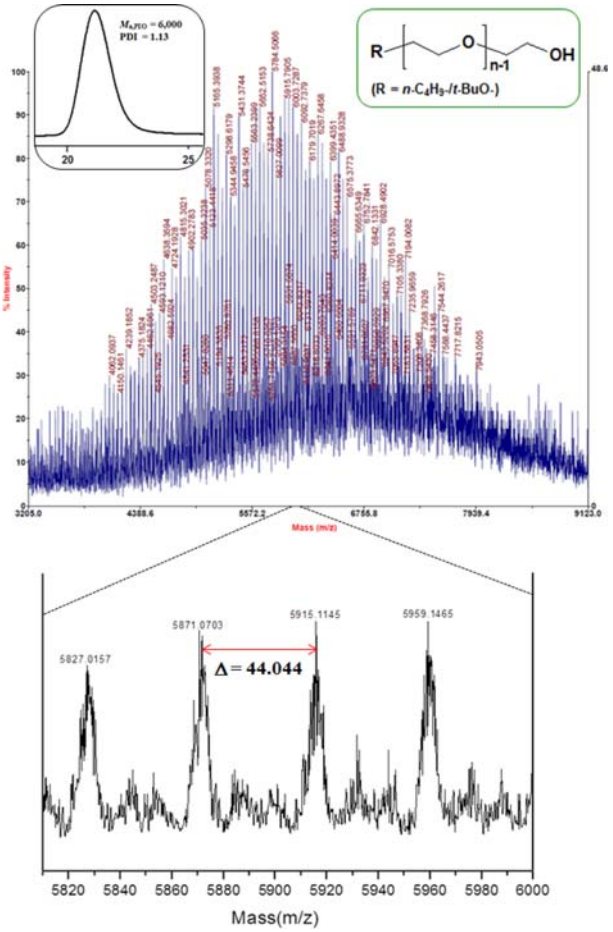


Figure 1. MALDI-TOF MS spectrum of R-PEO-OH (M_n=6,000) in the reflector mode and the subset presents the SEC of the corresponding *ω*-hydroxyl PEO.

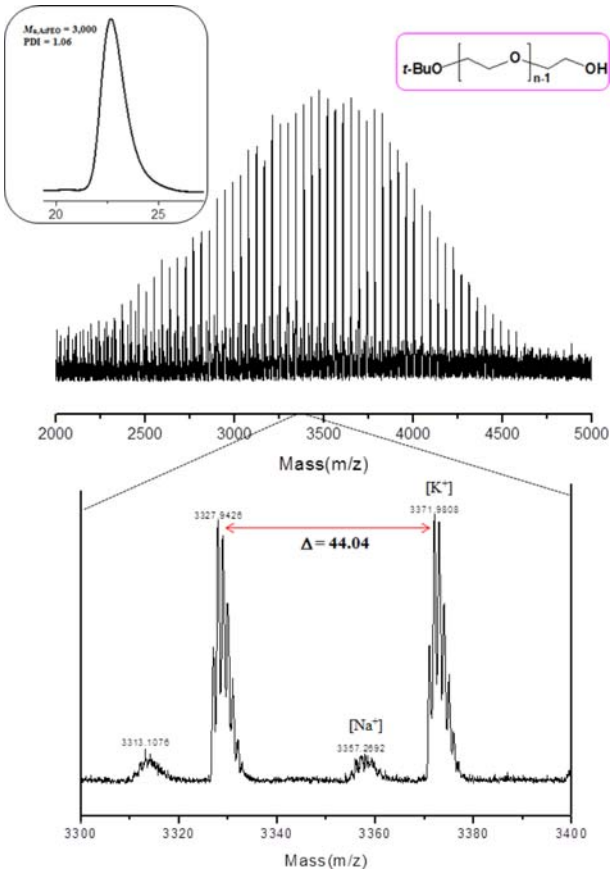
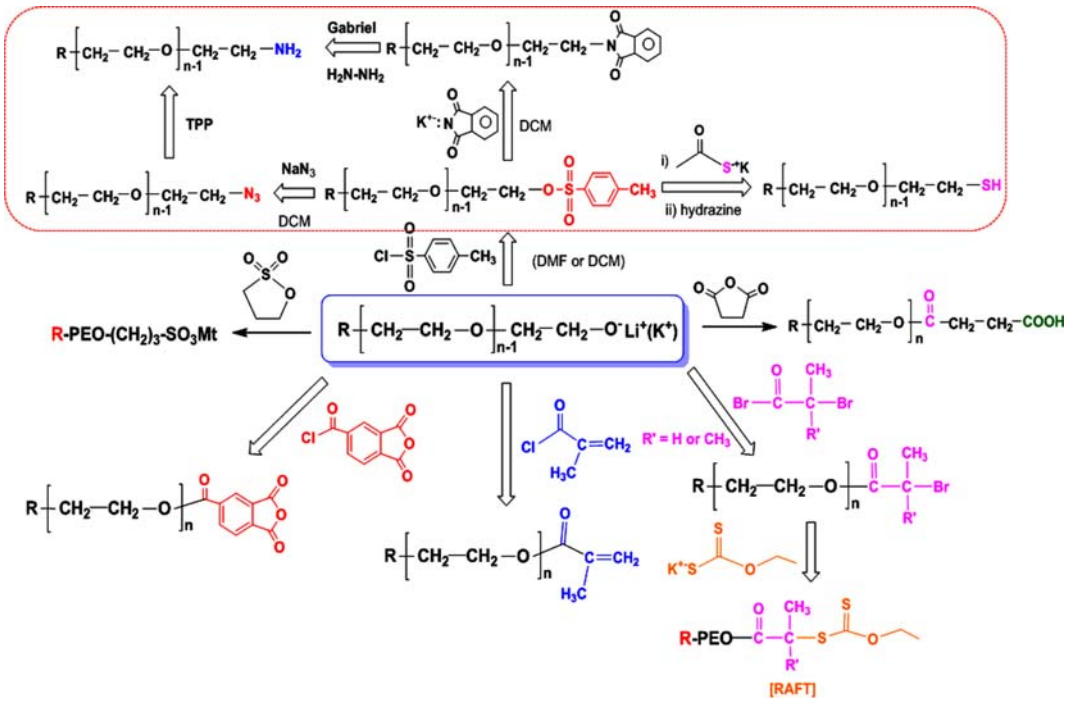


Figure 2. MALDI-TOF MS spectrum of *t*-BuO-PEO-OH in the reflector mode and the subset presents the SEC of the corresponding *ω*-hydroxyl *t*-BuO-PEO.

Chain-End Amination. It is well known that "living" polymerization is the best tool to synthesize *ω*-functionalized polymers.[22,28] The authors have reported that the PEO-based RAFT agent obtained from the chain-end functionalization of "living" polymeric alkoxide could be successfully used as a macroinitiator for the synthesis of a water-soluble thermoresponsive block copolymer.[29] As already mentioned, *n*-BuLi-initiated ring- opening polymerization of EO with *t*-BuOK in the mixture of benzene and DMSO (7/3, v/v) under a high vacuum seemed to generate "living" polymeric alkoxide, followed by chain-end termination as shown in Scheme I. As already mentioned, several other chain-end functionalizations including *ω*-bromination and *ω*-anhydride functionalization shown in Scheme I have been reported in the previous papers.[22,23,29] There are a number excellent reviews for the synthesis of heterobifunctional PEOs *via* ring-opening polymerization of EO using functional initiators.[30-33] To investigate whether quantitative chain-end functionalizations of polymeric alkoxide obtained from the above polymerization can be achieved or not, the amination, the azidolysis, and the thiolation of the polymeric alkoxide were employed in this study. In practice, all chain-end functionalizations were performed through the chain-end tosylation in DCM at 50 °C refluxing under inert gas, followed by further modifications. The tosylation yield was almost quantitative (over 98 mol%). Based on this result, a quantitative chain-end amination seemed to be achieved through the Gabriel process of PTI at the chain-end. Furthermore, *ω*-tosyl PEO was reacted not only with potassium PTI in DCM at 50 °C for 24 h leading to the production of *ω*-PTI PEO, but also with sodium azide yield-



Scheme I.

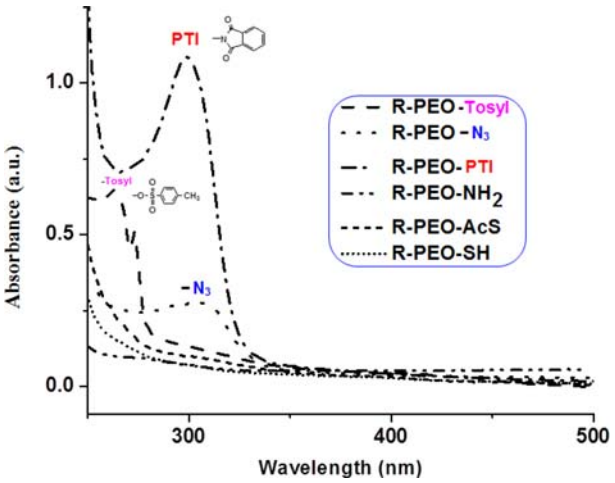


Figure 3. UV-Visible spectra of R-PEO-Tosyl, R-PEO-N_3, R-PEO-PTI, R-PEO-NH_2, and R-PEO-SH in distilled H_2O.

ing corresponding ω-azide PEO as shown in Scheme I.

In addition, it has been well known that the azide group can be readily converted to the corresponding ω-amine group from the reduction of azide by following the procedures described in the literature.[33-35] Figure 3 shows the UV-visible spectra of all products, R-PEO-Tosyl, R-PEO-N_3, R-PEO-PTI, R-PEO-NH_2, and R-PEO-SH in distilled H_2O. Clearly, the absorption maximum band at λ_{max}=285 nm of R-PEO-Tosyl appeared due to the chromophore of the phenyl ring on the tosylate group. The azidolysis and its imidation of R-PEO-Tosyl by the reaction with sodium azide and potassium PTI yielded corresponding R-PEO-N_3 and R-PEO-PTI, respectively. Concerning these functional groups, the absorption peak of the PTI group was observed at λ_{max}=305 nm in distilled H_2O, while *N*-methylphthalimide (NMP) as a model component exhibited theoretically the absorption at λ_{max}=281.89 nm in water.[36] The employment of the Gabriel process using hydrazine for amidation led to the complete disappearance of the maximum absorption band (R-PEO-PTI) at λ_{max}=305 nm. On the other hand, the azidolysis of ω-tosyl PEO by sodium azide (NaN_3) delivered new maximum absorption at λ_{max}=315 nm corresponding to the azide group from the absorption band at λ_{max}=285 nm (from the tosyl group). Furthermore, the absorption band of ω-tosyl PEO disappeared completely with thioacetylation in the vision region. All these observations revealed that the chain-end functionalization of polymeric alkoxide seemed to be achieved qualitatively through the modification of ω-tosyl PEO.

Next, the resulting ω-tosyl PEO was readily converted to both corresponding ω-amine PEO *via* the Gabriel process (deimidation) of the PTI group and corresponding ω-azide PEO by azidolysis, respectively. Figure 4 represents the typical ^{1}H NMR spectra of ω-tosyl PEO, corresponding ω-azide PEO, and corresponding ω-amine PEO directly obtained from the Gabriel process of ω-PTI PEO in $CDCl_3$. Simply, compari-

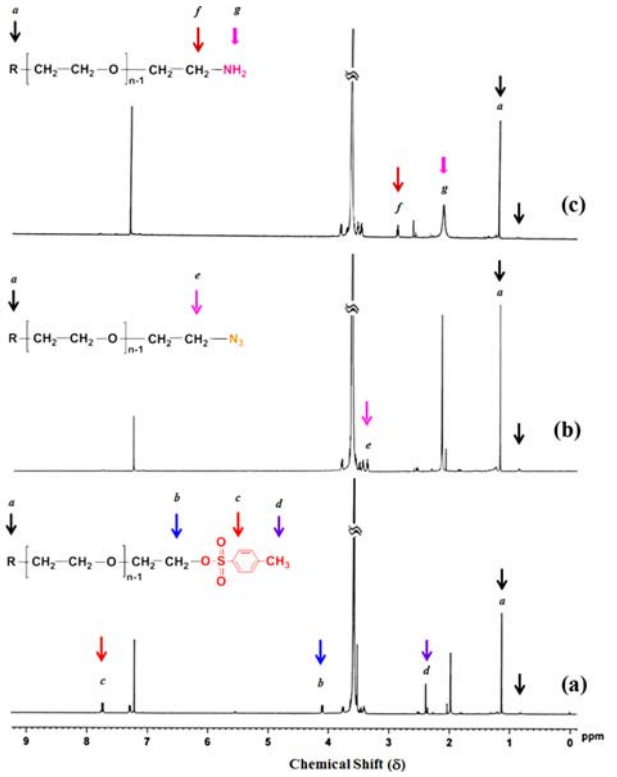


Figure 4. The ^{1}H NMR spectra of ω-tosyl PEO (a), corresponding ω-azide PEO (b), and corresponding ω-amine PEO directly obtained from ω-PTI PEO (c) in $CDCl_3$.

son of the integral intensities of all chemical shifts assigned in the ^{1}H NMR spectra exactly informed the corresponding functionalization yield as described in the other publication.[37] In Figure 4(a), the integrations of respective chemical shifts at δ=7.75 ppm and at δ=2.38 ppm assigned to the protons on the tosylate group indicate a quantitative tosylation yield (over 98 mol%). Furthermore, the chemical shift at δ=3.38 ppm corresponds to the protons on the methylene unit adjacent to the azide group in Figure 4(b), and the chemical shift at δ=2.88 ppm is assigned to the protons on the methylene unit adjacent to the amine group in Figure 4(c). Based on the results of the ^{1}H NMR spectral analysis, all functionalization yields for amination and azidation were over 98 mol%. In addition, Figure 5 shows the SECs of R-PEO (M_n=3,900), corresponding ω-tosyl PEO, corresponding ω-azide PEO, and corresponding ω-amine PEO directly obtained from ω-PTI PEO. The molecular weights of ω-azide PEO and ω-amine PEO look rather smaller than that of homo PEO. This phenomenon reveals that those PEOs act as polyelectrolytes exhibiting the different hydrodynamic volumes in polar solvents.[38]

As already mentioned, the reduction of the azide group using triphenyl phosphine (TPP) is well known for producing the corresponding amine group.[39] In practice, the ω-azido PEO was readily converted to the corresponding ω-amine PEO exhibiting a different structure to that shown in Figure

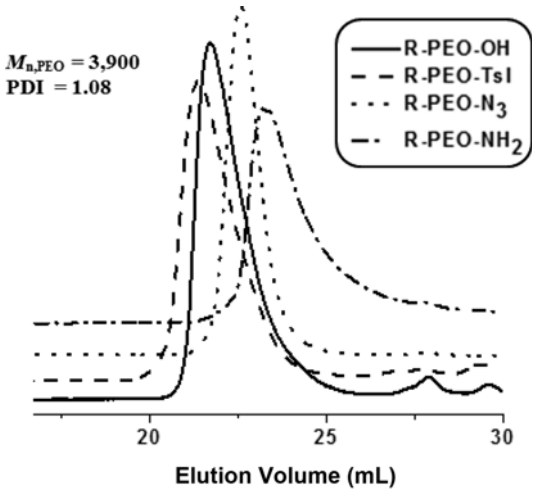


Figure 5. Size exclusion chromatograms of R-PEO (M_n=3,900), the corresponding ω-tosyl PEO, the corresponding ω-azide PEO, and the corresponding ω-amine PEO in THF as an eluent at 30 °C.

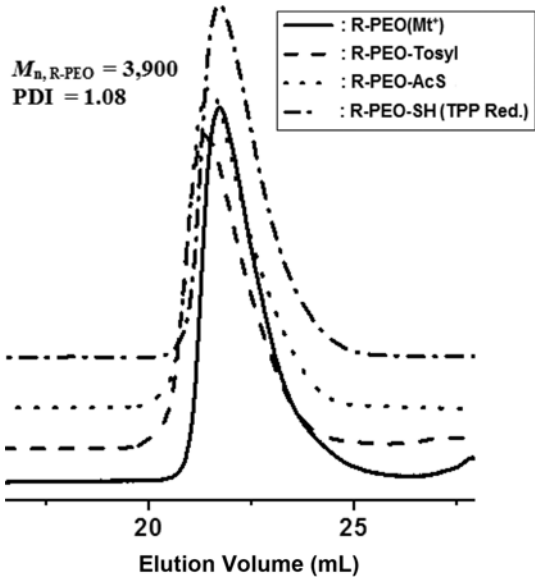


Figure 6. SECs of R-PEO (M_n=3,900 g/mol), the corresponding R-PEO-Tosyl, the corresponding ω-thioacetate PEO, and the corresponding ω-thiol PEO in THF as an eluent at 30 °C.

4(c) (see Figure S1 and Figure S2, Supporting Information). The original chemical shift at δ=3.38 ppm corresponding to the protons on the methylene unit adjacent to the azide group completely disappeared with the reduction, and the new appearance of the chemical shift at δ=3.18 ppm seemed to arise from the protons of the methylene unit adjacent to the primary amine group. However, it was slightly different from that of the compound obtained from the deimidation of the PTI group; that is, different chemical shifts at δ=2.88 ppm and at δ=3.18 ppm. This phenomenon was also observed in the case of the products obtained from the modification of *t*-BuO-PEO synthesized by *t*-BuOK-initiated polymerization of EO (see Figure S2, Supporting Information). In addition, the SECs of ω-azide *t*-BuO-PEO and ω-amine *t*-BuO-PEO showed monomodalities (see Figure S3, Supporting Information).

Chain-End Thiolation. To date, the employment of the thioacetate group as a precursor for the thiol group is expected to be the best tool to obtain ω-thiol polymers, followed by deacetylation.[33] As shown in Scheme I, ω-tosylate PEO reacted with potassium thioacetate in DMF at 50 °C for 24 h. The thioacetylation yield was over 98 mol%. Figure 6 is a comparison of the SECs of R-PEO, the corresponding R-PEO-Tosyl, the corresponding ω-thioacetate PEO, and the corresponding ω-thiol PEO eluted in THF. In this set, R-PEO and ω-tosylated PEO were the same compounds as those shown in Figure 5 and the corresponding ω-thioacetylated PEO and the corresponding ω-thiol PEO all look like monomodal distributions. The deacetylation process of the thioacetate group using excess hydrazine in methanol yielded 60 wt% of coupling of the deacetylated product (see Figure S4, Supporting Information). While this deacetylation process led to the formation of a relatively high fraction of the disulfide bond,[40] the reduction of the coupled product using TPP in methanol made the disulfide bond completely dissociated, which resulted in a monomodal distribution (as shown in Figure 6).[34] Figure 7 represents the ^{1}H NMR spectra of R-PEO (M_n=3,900 g/mol), the corresponding R-PEO-Tosyl, the corresponding ω-thioacetate PEO, and the corresponding ω-thiol PEO in $CDCl_3$. The chemical shifts of R-PEO-Tosyl in Figure 7(b) show analogous shapes to those of the spectrum in Figure 4(a). The chemical shift at δ=7.75 ppm assigned to the protons on the phenyl group of the tosylate group disappeared completely with thioacetylation leading to the generation of a new chemical shift at δ=3.12 ppm, which correspond to the protons on the methylene unit adjacent to the thioacetate group in Figure 7(c). Furthermore, the chemical shifts at δ=3.12 ppm and δ =2.35 ppm clearly disappeared with deacetylation in Figure 7(d). The new appearance of the chemical shift at δ=2.70 ppm indicates the formation of the thiol group at the chain end. In addition, the intensity of the chemical shift at δ=1.60 ppm corresponding to the proton on the thiol group was strong enough to monitor the proton on the that group. In summary, the chain-end thiolation was quantitative (over 98 mol%).

To our surprise, although the instability of the *t*-butoxy group under acidic conditions has been well documented in the literature,[41] that the hydrolysis of the initiating moiety (*i.e.*, the *t*-butoxy group among the initiating moieties) during the deacetylation process of the ω-thioacetate R-PEO under acidic conditions might take place in this study was completely overlooked. The authors did not expect absolutely that the hydrolysis of the *t*-butoxy group readily occurred because the deacetylation in the HCl/methanol solution yielded quantitative ω-thiol R-PEO in this study. In spite of a high thiolation yield, this deacetylation process yielded *ca.* 40 wt% of coupled products

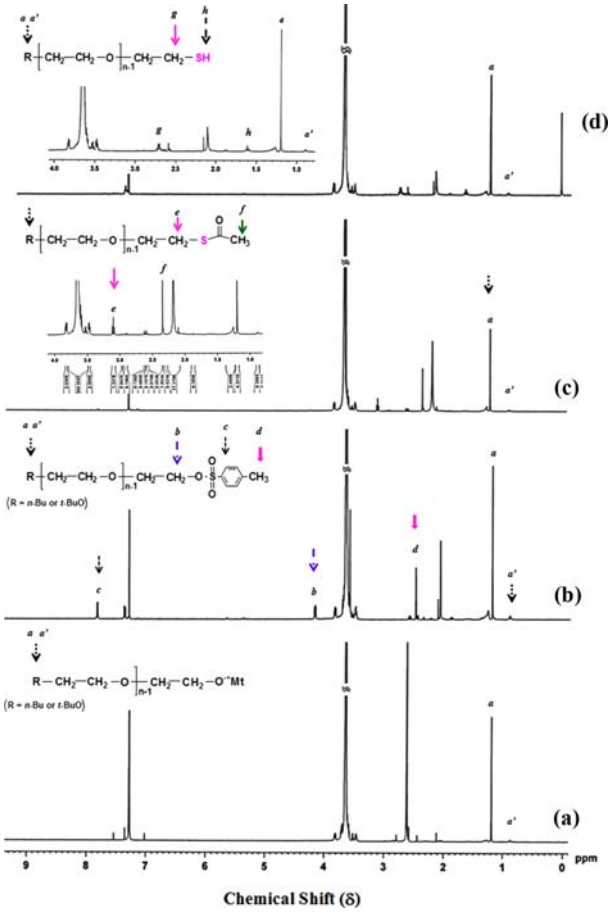


Figure 7. The ^{1}H NMR spectra of R-PEO (M_n=3,900), the corresponding R-PEO-Tosyl, the corresponding ω-thioacetate PEO, and the corresponding ω-thiol PEO in $CDCl_3$.

(disulfide) due to an oxidative coupling of the thiol group (see Figure S5, Supporting Information). The reduction of the disulfide bond using triphenylphosphine had to lead to the production of the corresponding thiol compound. The disulfide bond had to be dissociated leading to a monomodality of the product. In addition, thioacetylation of *t*-BuO-PEO quantitatively yielded ω-thioacetate *t*-BuO-PEO, followed by deacetylation in the HCl-methanol solution, which resulted in the formation of *ca*. 40 wt% of the coupled product (see Figure S6, Supporting Information). All thiolation yields were over 98 mol% on the basis of the result for the ^{1}H NMR spectral analysis. Unfortunately, among the initiating moieties (R) including the *n*-hexanoate moiety and the *t*-butoxy group, the main *t*-butoxy group seemed to disappear during the deacetylation process due to hydrolysis under acidic conditions on the basis of the results for the ^{1}H NMR analysis (see Figure S7, Supporting Information). The intensity of the chemical shift at δ=1.20 ppm that corresponded to the protons on the *t*-butoxy group unexpectedly decreased after deacetylation in the HCl/methanol solution while no change of the chemical shift at δ=0.88 ppm that corresponded to the protons on the methyl group of the *n*-hexanoate obtained from *n*-BuLi with one unit of EO was observed in $CDCl_3$ (see Figure S7(d), Supporting Information). This observation reveals that, even though this polymerization seems to be a very efficient method for obtaining PEOs with well-controlled molecular weight, further modification of the resulting PEO under acidic conditions should be limited due to hydrolysis of the *t*-butoxy group.[40] In particular, the hydrolyzed products were expected to exhibit the hydroxyl group at the chain end. The hydroxyl groups were monitored by ^{1}H NMR spectral analysis in deuterated DMSO (see Figure S8, Supporting Information). Clearly, both products in the cases of R-PEO-SH and *t*-BuO-PEO-SH show the chemical shift at δ=4.58 ppm, which corresponds to the proton on the hydroxyl group.

In addition, FTIR spectroscopic analysis for the functionalized PEOs provided the other excellent information for the formation of chain-end functionality (see Figure S9, Supporting Information). Azides show bands near 2140 cm^{-1} due to the resonance form with cumulated double bonds. Concerning this behavior, only ω-azide R-PEO show bands near 2140 cm^{-1}. The other spectra do not show any different stretching frequencies.

Conclusions

We have developed a useful and powerful method to control the molecular weight of PEO and to achieve a quantitative chain-end functionalization yield *via* an anionic mechanism. Specifically, the cost-effective and authentic alkyllithium-initiated ring-opening polymerization of EO can produce the corresponding polymeric alkoxide with a predicted molecular weight based on the stoichiometric balance (M_n=monomer(g)/{x×[BuLi]+y·[*t*-BuOK]}). The resulting alkoxide is active enough to be further modified because all the growing species exhibited a "living" nature. The chain- end functionalizations, such as amination, azidation, and thiolation, were readily carried out using ω-tosylate PEO as an intermediate, which was synthesized by the reaction of the active polymeric alkoxide with *p*-toluenesulfonyl chloride. All functionalization yields were quantitative (over 98 mol% on the basis of ^{1}H NMR analysis). In particular, among the initiating moieties (*n*-hexanoate and *t*-butoxide), the *t*-butoxide group was found to be susceptible for hydrolysis under acidic conditions. In this respect, all reactions should be controlled under basic conditions.

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Supporting Information: Experimental results and additional figures. The materials are available *via* the Internet at http://www.springer.com/13233.

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