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N-Heterocyclic Carbene-Induced Zwitterionic Ring-Opening Polymerization of Ethylene Oxide and Direct Synthesis of α,ω-Difunctionalized Poly(ethylene oxide)s and Poly(ethylene oxide)-*b*-poly(ε-caprolactone) Block Copolymers

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Abstract: An N-heterocyclic carbene (NHC), namely, 1,3-bis-(diisopropyl)imidazol-2-ylidene (**1**), was demonstrated to bring about the metal-free ring-opening polymerization of ethylene oxide at 50 °C in dimethyl sulfoxide, in absence of any other reagents. Poly(ethylene oxide) (PEO) of polydispersities <1.2 and molar masses perfectly matching the [monomer]/[(**1**)] ratio could thus be obtained in quantitative yields, attesting to the controlled/living character of such carbene-initiated polymerizations. It is argued that (**1**) adds to ethylene oxide to form a zwitterionic species, namely 1,3-bis-(diisopropyl)imidazol-2-ylidinium alkoxide, that further propagates by a zwitterionic ring-opening polymerization (ZROP) mechanism. Through an appropriate choice of terminating agent NuH or $NuSiMe_3$ at the completion of the polymerization, a variety of end-functionalized PEO chains could be generated. In particular, α,ω-bis(hydroxy)-telechelic PEO, α-benzyl,ω-hydroxy, and α-azido,ω-hydroxy-difunctionalized PEOs were synthesized by NHC (**1**)-initiated ZROP, using H_2O, $PhCH_2OH$, and N_3SiMe_3 as terminating agent, respectively. Characterization of these α,ω-difunctionalized PEOs by techniques such as ^{1}H NMR spectroscopy, MALDI-TOF spectrometry, and size exclusion chromatography confirmed the quantitative introduction of functional groups at both α and ω positions of the PEO chains and the formation of very narrow molar mass polymers. Finally, the synthesis of a poly(ethylene oxide)-*b*-poly(ε-caprolactone) diblock copolymer by sequential ZROP of the corresponding monomers was successfully achieved using (**1**) as organic initiator without isolation of the PEO block intermediate.

Introduction

Poly(ethylene oxide) (PEO), also referred to as poly(ethylene glycol) (PEG), is the reference biocompatible polymer used in the biomedical field as a result of its unique properties, namely, its chemical stability, solubility in both organic and aqueous media, nontoxicity, low immunogenicity, and antigenicity.[1] PEG derivatives have been widely used as conjugates (PEGylation reaction) to increase the circulation half-life of biologically active molecules (e.g., enzymes, peptides, proteins), to improve the solubility of various anticancer agents (e.g., taxol or camptothecin), and to impart enhanced permeability and retention and increase passive targeting of anticancer drugs.[2−5] PEG is also used as an efficient spacer in delivery systems such as PEG-grafted liposomes and nanoparticles. Several PEG-conjugated proteins are already available as clinical therapeutics.[6] In addition to these biomedical applications, PEG also serves as an inert support in liquid-phase organic synthesis.[7] Applications of PEO, however, often require α,ω-heterodifunctional PEO-based oligomers possessing tailored reactive end functions such as amine, carboxylic, thiol, aldehyde, or maleimide to react with a variety of ligands.[6,8−18]

From a synthetic and mechanistic point of view, the elucidation of the ring-opening polymerization of ethylene oxide by Flory dates back to the early 1940s.[19,20] Linear PEOs are commonly obtained by anionic ring-opening polymerization (AROP) of ethylene oxide from alkali metal alkoxide initiators, under dry and inert atmosphere.[21−25] AROP of ethylene oxide (EO) thus involves propagating alkoxides with an admittedly low rate of polymerization, and the reactivity of alkoxides depends on metallic countercation (higher reactivity in the order $Na^+ < K^+ < Cs^+$).[23,24,26] As for heterodifunctional PEOs, they can be synthesized using the two following strategies. The first one consists in direct AROP of EO from α,ω-heterodifunctional alkali metal-based initiators, followed by the addition of an appropriate functionalized terminating agent. However, this method often requires that one functional group be protected.[1]

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The second method is based on the derivatization of an α,ω-bis(hydroxyl)-telechelic PEO precursor, followed by a tedious separation step of the resulting mixture of mono-, di-, and unsubstituted PEOs.[1] As a matter of fact, only a few examples[8,27−29] of simple synthetic routes to α,ω-functionalized PEOs have been reported. Thus, a versatile and straightforward synthetic pathway that gives access to heterodifunctional PEOs and that meets the criteria of control over molar masses and polydispersities (PDs), simplicity of polymerization process, and PEO chain-end functionalization is needed.

Moreover, the removal of metallic contaminants introduced by the initiator is a necessity in most of the applications involving PEO, in a context where environment-benign materials are more than ever searched for. The replacement of metallic initiators by purely organic and less toxic species in polymerizations such as AROP of EO is an appealing option.

We wish to report here about the ability of an N-heterocyclic carbene (NHC), namely, 1,3-bis-(diisopropyl)imidazol-2-ylidene (**1**), to bring about a metal-free living polymerization of EO. In addition to their role as efficient ligands of transition-metal complexes in organometallic reactions,[30,31] NHCs have also emerged as highly efficient organic catalysts for various reactions in molecular chemistry.[32−37] The reason for their success has to be found in their structural diversity: NHCs can indeed challenge most metal-based or enzymatic catalysts.[36,37] It is worth pointing out that NHCs have been mainly used in reactions involving an activation of carbonyl moieties. One of the best illustrations of such carbonyl-activated reactions is the NHC-catalyzed ROP of cyclic esters by Hedrick et al.[38−47] However, NHCs can also activate other electrophilic groups such as trialkylsilyl groups for cyanosilylation or trifluoromethylsilylation of ketones and/or aldehydes.[48−53] On this basis, both Hedrick et al.[54] and our group[55] recently showed that NHCs can catalyze silyl ketene acetals and trigger living group transfer polymerization of both methacrylic and acrylic monomers. Use of NHCs as organocatalysts for ROP of EO carried out in the presence of an alcohol as a real initiator was briefly described by Hedrick et al.[56] Here, we propose that NHC **1** can directly attack EO to form a metal-free imidazolium alkoxide that propagates PEO chains by a zwitterionic ring-opening polymerization (ZROP) mechanism. Through the use of appropriate terminating agents NuH or $NuSiMe_3$ (e.g., Nu = HO-, N_3-, or $PhCH_2O$-) to deactivate such a metal-free polymerization, telechelic of heterodifunctional PEOs becomes accessible in a very versatile fashion, combining excellent control of molar masses, narrow polydispersities, and quantitative chain-end

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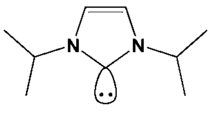
Table 1. Polymerizations of EO Initiated by NHC **1** in DMSO at 50 °C

expt	V_{EO} (mL)	m_{NHC} (mg)	conv (%)	th M_n[a]	expt M_n[b]	PD[b] (M_w/M_n)	TA[c]
1	1	50	30	800	oligomers		H_2O
2	1	50	100	2700	2500	1.11	H_2O
3	1	30	100	4500	4700	1.05	H_2O
4	1	20	100	6700	8200	1.02	H_2O
5	1	10	100	13400	12800	1.03	H_2O
6	1	50	100	2700	2400	1.11	$PhCH_2OH$
7	1	50	100	2700	2300	1.14	$N_3{-}SiMe_3$
8[d]	1	20	100	6700	6800	1.07	H_2O
	+1 mL εCL		50	11100	10400	1.08	

[a] Theoretical molar masses: th M_n = ([monomer]/[I])·conv·M_{MU} + M_I, where M_{MU} and M_I are the molar masses of the monomer unit and the initiator, NHC in this case, and conv is the monomer conversion determined by gravimetry. [b] Experimental molar masses and PD obtained by SEC in THF using poly(ethylene oxide) standards for calibration. [c] TA stands for termination agent. [d] Copolymerization of EO and εCL. The living PEO chains are used to initiate the second block of PCL, and the molar masses take into account both blocks.

functionalization. We finally show that the sequential ZROP of EO and ε-caprolactone initiated by **1** affords a well-defined poly(ethylene oxide)-*b*-poly(ε-caprolactone) block copolymer through a one-pot and easy procedure.



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Experimental Section

Materials. EO (Fluka, 99.8%) was distilled over sodium into a burette. All other reagents were purchased from Aldrich. Dimethyl sulfoxide (DMSO) was distilled over CaH_2 before use following a minimum of 5 h of reflux. Tetrahydrofuran (THF) was distilled over sodium/benzophenone to prepare solutions of NHC **1**. ε-Caprolactone (ε-CL) was distilled over CaH_2 and then stored in a burette. Benzyl alcohol was distilled and stored over molecular sieves. Trimethylsilyl azide was dried and distilled over CaH_2. NHC **1** was prepared by slightly modifying already reported procedures:[57] the diisopropyl-imidazolium salt was deprotonated with NaH and a catalytic amount of *t*BuOK. Then, NHC **1** was purified by distillation under vacuum. Solutions of this catalyst were kept in a glovebox under argon atmosphere.

Synthesis of α,ω-Difunctionalized Poly(ethylene oxide)s. Polymerization of EO was carried out under a dry and inert atmosphere using Schlenk equipment. In a typical polymerization, 2 mL of a 10^{-1} M solution of NHC **1** (2×10^{-4} mol) (entry 3, Table 1) was introduced via a syringe in a vacuumed flame-dried Schlenk kept in a glovebox under an argon atmosphere. After removal of the Schlenk from the glovebox, 15 mL of dry DMSO was added under vacuum. After homogenization, 1 mL (5×10^{-2} mol) of EO was introduced at −20 °C. The Schlenk was allowed to warm to room temperature and set in a thermostatted oil bath at 50 °C for 3 days. After a couple of minutes, the color turned orange, likely characteristic of an imidazolium alkoxide. Three equivalents relative to NHC of an appropriate terminating agent (deionized H_2O, N_3SiMe_3, or $PhCH_2OH$) were then introduced. The color turned pale yellow, and the reaction mixture was stirred overnight. The DMSO solution was precipitated in a large excess of diethyl ether at room temperature. The polymer was redissolved in dichloromethane and precipitated twice in diethyl ether and recovered as a white powder that was dried under vacuum. Molecular characteristics of all NHC-derived PEOs are provided in Table 1.

Hydroxytelechelic PEO with 4700 g/mol (SEC THF), $D = 1.05$, ^{1}H (DMSO-d_6) 3.5 ppm ($C\underline{H_2}O{-}$) and 4.55 ppm ($-OCH_2CH_2O\underline{H}$); α-$C_6H_5CH_2O$,ω-OH-functionalized PEO with 2400 g/mol (SEC), PD = 1.11, ^{1}H 3.5 ppm ($C\underline{H_2}O{-}$), 7.3 ppm ($C_6\underline{H_5}{-}CH_2O$), 4.5 ppm ($C_6H_5{-}C\underline{H_2}O$), and 4.55 ppm ($-OCH_2CH_2O\underline{H}$); α-$N_3$,ω-OH-functionalized PEO with 2300 g/mol (SEC), PD = 1.14, ^{1}H 3.5 ppm ($C\underline{H_2}O{-}$), 3.4 ppm ($N_3{-}C\underline{H_2}CH_2O$), and 4.55 ppm ($-OCH_2CH_2O\underline{H}$), ^{13}C (DMSO-$d_6$) 70.6 ppm ($\underline{C}H_2O{-}$), 50.9 ppm ($N_3{-}\underline{C}H_2CH_2O$), 73.2 ppm ($-OCH_2\underline{C}H_2OH$), and 61 ppm ($-O\underline{C}H_2CH_2OH$).

Synthesis of Poly(ethylene oxide)-*b*-poly(ε-caprolactone) Block Copolymers by Sequential Polymerization. The PEO block was first grown, following strictly the same procedure as that described above. For instance, 1.3 mL of a 10^{-1} M solution of **1** (1.3×10^{-4} mol or 20 mg) (entry 8 in Table 1), 10 mL of DMSO, and then 1 mL (5×10^{-2} mol) of EO were added to a flame-dried Schlenk. After 72 h, an aliquot (∼0.1 mL) was withdrawn for size exclusion chromatography (SEC) characterization and the rest of the solution was treated as follows, that is, without isolation of the PEO first block. One milliliter (9×10^{-3} mol) of εCL was added to the previous solution, and the polymerization was resumed for another 24 h at 50 °C. The polymerization time was voluntarily not prolonged to avoid reaching completion of the reaction and therefore favoring the back-biting side reaction that occurs at high conversion.

Characterization. ^{1}H NMR spectra were recorded on a Bruker AC 400 spectrometer. Molar masses of PEO samples were determined by SEC that was performed using a three-column set of TSK gel TOSOH (G4000, G3000, G2000) calibrated with PEO standards with THF as eluent eluent (1 mL/min) and trichlorobenzene as a flow marker at 25 °C. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry was performed using a Voyager-DE STR (Applied Biosystems) spectrometer equipped with a nitrogen laser (337 nm), a delay extraction, and a reflector. The MALDI mass spectra represent averages over 100 laser shots. This instrument operated at an accelerating potential of 20 kV. The polymer solutions (10 g L^{-1}) were prepared in CH_2Cl_2. The matrix solution (1,8-dithranol-9(10*H*)-anthracenone, dithranol) was dissolved in CH_2Cl_2. The polymer solution (2 μL) was mixed with 20 μL of the matrix solution, and 2 μL of a sodium iodide solution (10 g L^{-1} in methanol) was added to favor ionization by cation attachment. The final solution (1 μL) was deposited onto the sample target and dried in air at room temperature. Infrared measurements were performed on a Bruker Tensor 27 spectrometer using the attenuated total reflection method from films obtained with CH_2Cl_2 as solvent.

Results and Discussion

The polymerization of ethylene oxide was triggered by addition of 1,3-bis-(diisopropyl)imidazol-2-ylidene (**1**), an NHC used here as a direct organic initiator in the absence of any other reagents. NHC **1** was selected for its ease of synthesis and purification by distillation, which affords an organic initiator free of any metallic residues. We preferred to handle such a "bare" NHC rather than generate it in situ by deprotonation of the corresponding imidazolium with a base (e.g., *t*BuOK, NaH, or BuLi) which might have interfered with the polymerization of EO and introduced metallic contaminants in the resulting PEOs. ROP of EO is a relatively slow process.[20−23] We first observed that almost no polymer was formed when using THF as solvent at room temperature. In contrast, near-quantitative yields were obtained by carrying out the polymerization at 50 °C in a more dissociating solvent such as DMSO (Table 1). After several minutes of reaction between EO and NHC **1**, the color of the solution turned slightly orange, indicative of the formation of imidazolium alkoxide (Scheme 1), and tended to deepen in the course of the reaction. A few drops of water were added to discontinue the polymerization after 72 h; as discussed

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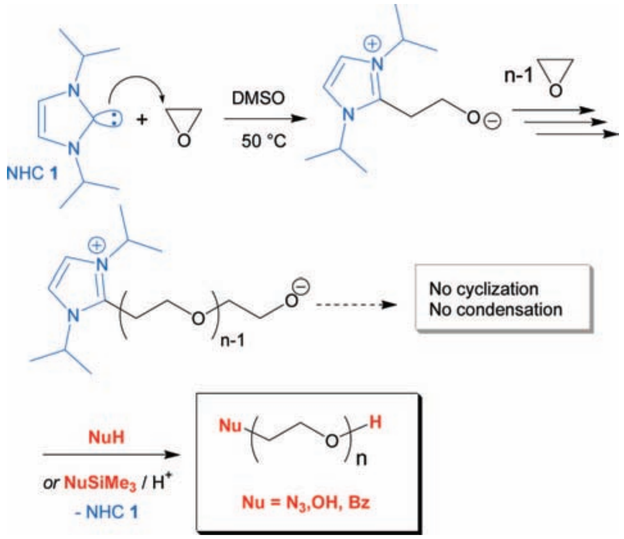
Scheme 1. Proposed Mechanism of Zwitterionic Ring-Opening Polymerization of Ethylene Oxide



later, other judiciously chosen functional chain terminators were also used to derive α,*ω*-difunctionalized (heterotelechelic) PEOs. The molar masses of the PEOs were found to remarkably coincide with the targeted values based on the initial [EO]/[**1**] molar ratios, with polydispersities remaining lower than 1.2 (Figure 1), which is consistent with a controlled/living process over a range of different molar masses (Table 1). A slight asymmetry can be observed in the SEC trace of experiment 2 (Figure 1). The slight tailing appearing in the low molar masses area (also observed on Figures 4 and 5) is likely to be due to the power of separation of the oligomers by the set of three SEC columns. As a matter of fact, low molar mass species are emphasized. This is particularly prominent on the SEC trace in Figure 1, where the different oligomers appear as discrete peaks with molar masses that are separated by only one monomer unit.

The formation of linear PEOs from NHC **1** as organic initiator occurs very likely via an initial nucleophilic attack of **1** onto one methylene group of EO, resulting in the generation of 1,3-bis-(diisopropyl)imidazol-2-ylidinium alkoxide. The latter species is nucleophilic enough to propagate PEO chains by a ZROP mechanism until complete conversion of EO (Scheme 1). The imidazolium moiety plays here the role of the countercation allowing further propagation. Zwitterionic polymerizations of monomers such as alkyl oxazolines, cyanoacrylates, or *N*-carboxyanhydrides have been known for a while,[58−64] but to the best of our knowledge, such a mechanism has not been reported in the case of ROP of EO. Recently, Hedrick et al. demonstrated that NHC-initiated polymerization of lactide also occurs through ZROP, which was exploited to selectively generate cyclic biodegradable polylactides of quite high molar masses and narrow polydispersities.[45] Living zwitterionic PEO chains can undergo intramolecular cyclizations leading to macrocyclic PEOs or intermolecular condensation reactions as well. Under the conditions described above, however, ZROP of EO gave exclusively rise to linear PEOs exhibiting a unimodal distribution of molar masses only, with no evidence for cyclic polymers or of polycondensates. The linear structure of these PEOs was checked by a combination of techniques, including ^1H NMR spectroscopy, SEC, and MALDI-TOF mass spectrometry (see below).

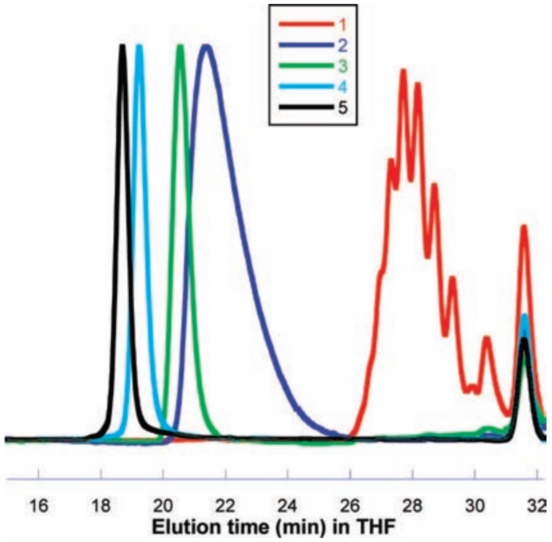


Figure 1. SEC traces (RI detection) of PEOs (entries 1−5, Table 1).

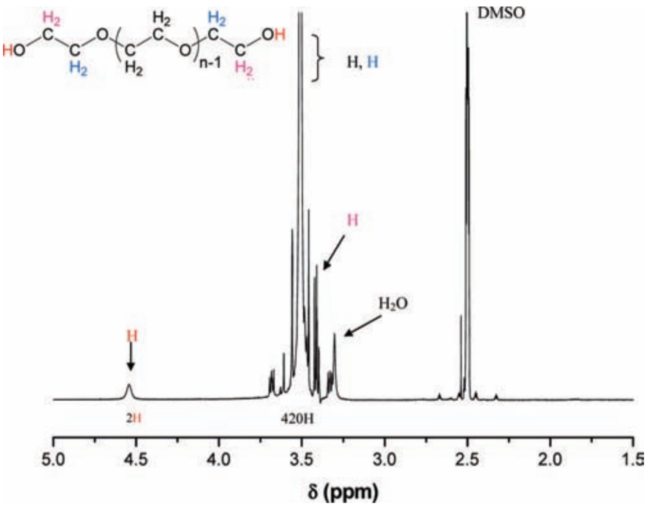


Figure 2. ^1H NMR spectrum of α,*ω*-bis(hydroxy) PEO (entry 3, Table 1).

The first series of PEOs obtained was neutralized by simple addition of H_2O used as terminating agent and was characterized by ^1H NMR spectroscopy in DMSO-d_6. In this case, it is expected that hydroxide (OH^-) behaves as a nucleophile that displaces the α-imidazolium moiety from PEO chains, thus releasing the NHC, whereas the *ω*-alkoxide end is transformed into a *ω*-hydroxy function. In other words, the use of H_2O as chain stopper in ZROP of EO is due to generate α,*ω*-bis(hydroxyl)-telechelic PEOs. Figure 2 shows a typical ^1H NMR spectrum of such H_2O-terminated PEO (entry 3, Table 1) with all peak assignments. All the expected peaks are observed, in particular, the one due to the resonance of the two terminal hydroxyls at 4.55 ppm. The relative integration of this peak to that characteristic of the protons of PEO chains at 3.5 ppm provides another means to determine the molar mass of

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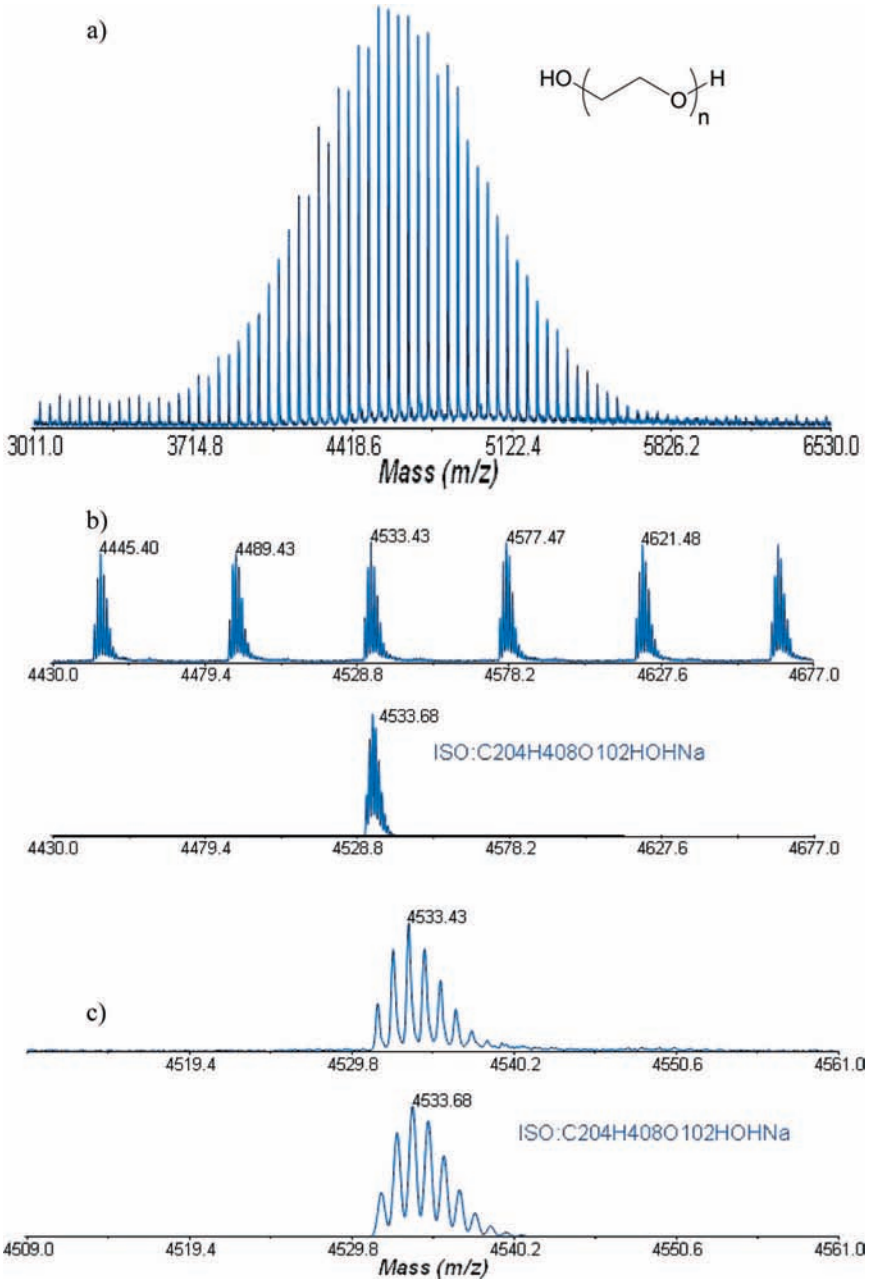

Figure 3. MALDI-TOF mass spectrum of α,ω-bis(hydroxy) PEO (entry 3, Table 1).

these samples, assuming the presence of two terminal hydroxyls per PEO chain. The molar mass value calculated (4620 g/mol) by this means is very close to the value previously determined by SEC (4700 g/mol) and to that predicted by the molar ratio of EO to NHC initiator **1** (4500 g/mol). This confirmed that two hydroxyl functions were quantitatively introduced at PEO chain ends in such NHC-mediated ZROP of EO deactivated by water. The NHC thus released after termination of ZROP is supposedly deactivated by water,[65] the byproduct being eliminated in diethyl ether used to precipitate the PEO, though it was not attempted to analyze further the residues formed.

The use of difunctional terminating agents (other than water) for the ZROP of EO was investigated next, with the view of generating miscellaneous α,ω-bifunctionalized PEO telechelics in a simple manner. Considering that the terminating agents of general structure NuH or NuSiMe$_3$ can bring about a nucleophilic attack on the imidazolium moiety resulting in the substitution of Nu$^{\delta-}$ and that the primary alkoxide carried by the chain end can concomitantly react with H$^{\delta+}$ or Me$_3$Si$^{\delta+}$ (Scheme 1), an obvious choice is to resort to an alcohol. We turned to benzyl alcohol (PhCH$_2$OH) since the benzyl group (Bz) is easily revealed by ^{1}H NMR, MALDI-TOF spectroscopy, or by UV through the response in the SEC trace of the corresponding PEO. In the corresponding ^{1}H NMR spectrum (Figure 4 and entry 6, Table 1), indeed, characteristic protons of both benzyl and hydroxyl end groups could be clearly identified, at 7.3 ppm ($C_6\underline{H_5}-CH_2O$), 4.5 ppm ($C_6H_5-C\underline{H_2}O$), and 4.55 ppm ($-OCH_2CH_2O\underline{H}$), respectively. The integration of these peaks compared to that due to protons of the PEO main chain gave an M_n value of 2420 g/mol, in excellent agreement

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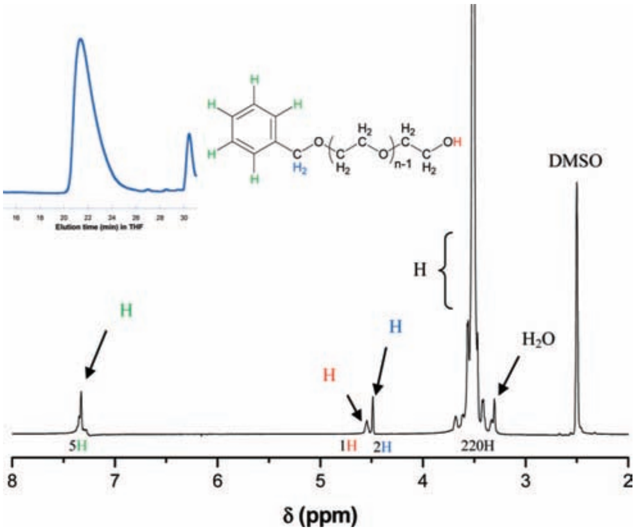

Figure 4. ^{1}H NMR spectrum and SEC trace (RI detection on top left) of α-benzyl,*ω*-hydroxy PEO (entry 6, Table 1).

with the one obtained by SEC (2400 g/mol). In addition, the UV signal observed at 254 nm, though relatively weak, confirmed the introduction of the benzyl group in this PEO sample. These results indicate that benzyl alcohol can well be used to terminate the living ZROP of EO, with no side reaction detected. It can thus be inferred that many other OH-containing terminating agents could be utilized to generate α,*ω*-hydroxy-bifunctionalized PEOs; work is in progress toward this objective.

To broaden the choice of reactive functions that could end-cap PEO chains derived from NHC-initiated ZROP, we turned to the commercially available trimethylsilyl azide (N_3SiMe_3) as terminating agent, the alkoxides carried by the living ends being known as silicophilic.[66] Interestingly, with such an end-capping agent an azido function is directly introduced in the α-position of PEO chains, thus generating α-azido,*ω*-trimethylsilyloxy-bifunctionalized PEOs that can be readily transformed into α-azido,*ω*-hydroxy-bifunctionalized PEOs by simple acidic treatment (Experimental Section). Organic azides recently received considerable attention in different areas of chemistry owing to their ability to readily react with alkynes by Huisgen 1,3-dipolar cycloaddition known as “click chemistry” to afford 1,2,3-triazole groups. More generally speaking, this click reaction is a versatile method of creating C−C bonds (or C−N), under mild experimental conditions, combining tolerance of functional groups and high yields.[67−70] Click chemistry has been recognized as a powerful tool not only in macromolecular engineering, but also in the field of bioconjugate chemistry.[71−73] In the case of the heterodifunctionalization of PEO, little attention has been given to versatile synthetic methods that deliver azido-terminated PEOs.[1] For instance, Hiki and Kataoka recently reported on the synthesis of azido-terminated PEOs using allyl alcohol as heterodifunctional precursor.[15] Though very efficient, this method utilizes an alkali metal-based initiator and also requires a two-step modification of the hydroxyl end into an azido group. We propose here to directly use N_3SiMe_3 as terminator for PEO chains at the completion of the NHC-mediated ZROP of EO as a one-pot and very simple route to azido-terminated heterodifunctional PEOs. Figure 6, indeed, shows the ^{1}H NMR spectrum and the SEC trace of the resulting PEO (see also entry 7 in Table 1). The peak due to the resonance of methylene in α-position to the azido group ($-C\underline{H_2}N_3$) appears as a triplet at 3.4 ppm, as previously reported.[15] Characterization of this sample by ^{13}C NMR confirms the presence of the azido group through the appearance of a peak at 50.9 ppm due to the carbon atom of $-\underline{C}H_2N_3$ carrying the azido group.[15] The introduction of the azido function is also supported by FTIR analysis, which shows a characteristic signal at 2100 cm^{-1} (Figure 8). Here again, the experimental molar masses determined by ^{1}H NMR (2300 g/mol) or by SEC (2200 g/mol) are in good concordance with theoretical value ($M_{n,theo} = 2700$ g/mol), while polydispersity is close to unity (PD = 1.14). Because the $O-SiMe_3$ group is labile, it has to be stressed that access to the OH moiety is easy, requiring a simple hydrolysis (HCl/EtOH) which also helps the recovery of the OH-terminated PEO by precipitation (without terminal hydroxyl group, PEO is difficult to precipitate out from diethyl ether). This explains why hydroxyl functions rather than $O-SiMe_3$ groups were observed at PEO chain ends when using N_3SiMe_3 as deactivating agent.

Further evidence of the expected structure and the quantitative functionalization of PEO chain ends was provided by MALDI-TOF mass spectrometry (Figures 3, 5, and 7). Each of the three samples analyzed shows both narrow molar mass distributions and the molecular ion corresponding to the linear PEO complexed by sodium. One single distribution is indeed observed for both the α,*ω*-bis(hydroxyl)-telechelic PEO and the α-benzyl,*ω*-hydroxy PEO (Figures 3 and 5), while an overlap of two distinct populations is seen for the α-azido,*ω*-hydroxy-difunctionalized PEO (Figure 7). In the latter case, the expected population with its N_3 functionality is clearly observed but a second population arises due to a loss of molecular N_2 by fragmentation, which certainly occurs during the ionization process. For each population observed in the MALDI-TOF mass spectrum of the three samples, one can observe a peak-to-peak mass increment of 44.05 g/mol corresponding to the molar mass of one EO unit. In all cases, the distribution of chain can thus be perfectly accounted for, taking into account the molar mass of both the core and chain ends. The peaks, indeed, appear at $m/z = 44.05n + M_{termi} + 23$, where n is the degree of polymerization, 23 is the molar mass of the sodium ion generated during the ionization process, and M_{termi} is the molar mass of end groups. As illustrated in Figures 3, 5, and 7, the experimental and the theoretical isotope distributions are in perfect agreement, all signals being attributed to the cationized adduct of the expected α,*ω*-bifunctionalized PEO. It is noteworthy that the values of molar masses and polydispersities thus obtained by MALDI-TOF mass spectrometry (respectively, 4600 g/mol and 1.06 for α,*ω*-bis(hydroxyl)-telechelic PEO, 2100 g/mol and 1.1 for α-benzyl,*ω*-hydroxy PEO, 2000 g/mol and 1.15 for α-azido,*ω*-hydroxy PEO) are also very close to those determined by SEC and by ^{1}H NMR spectroscopy, as discussed above. Importantly, no other series of products carrying defects with respect to the terminal functions can be detected and no

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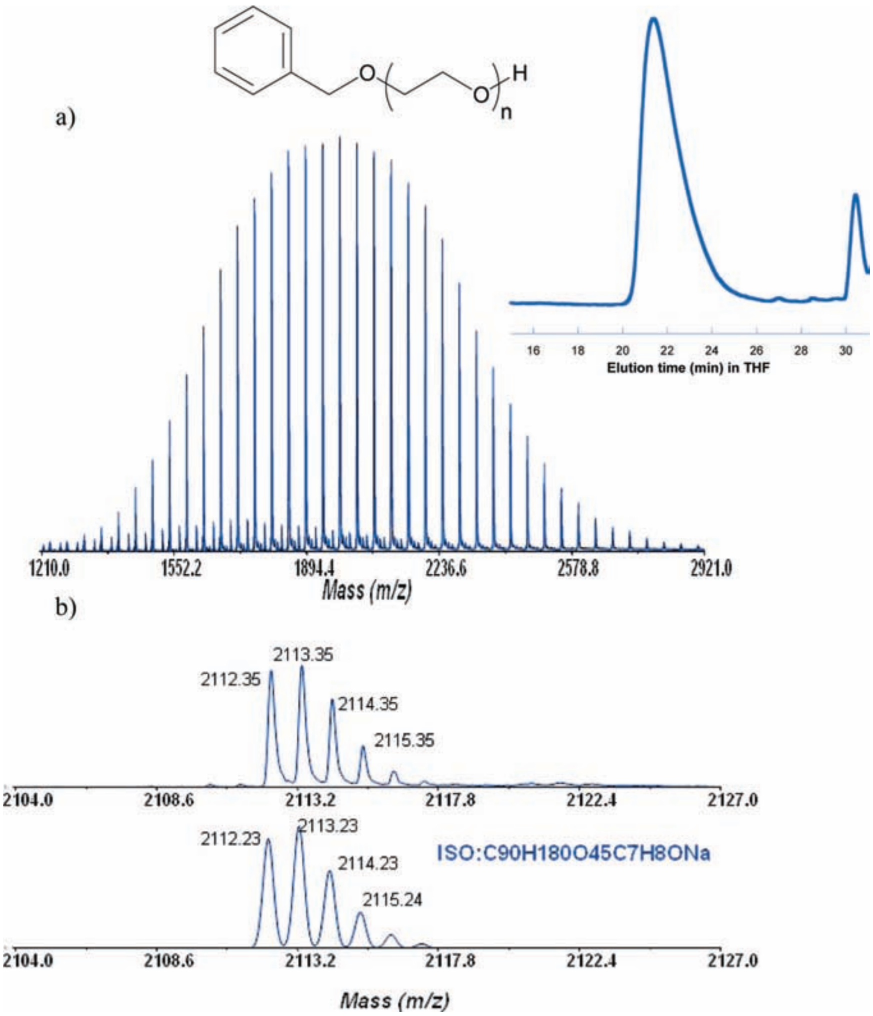

Figure 5. MALDI-TOF mass spectrum and SEC trace (RI detection on top right) of α-benzyl,*ω*-hydroxy PEO (entry 6, Table 1).

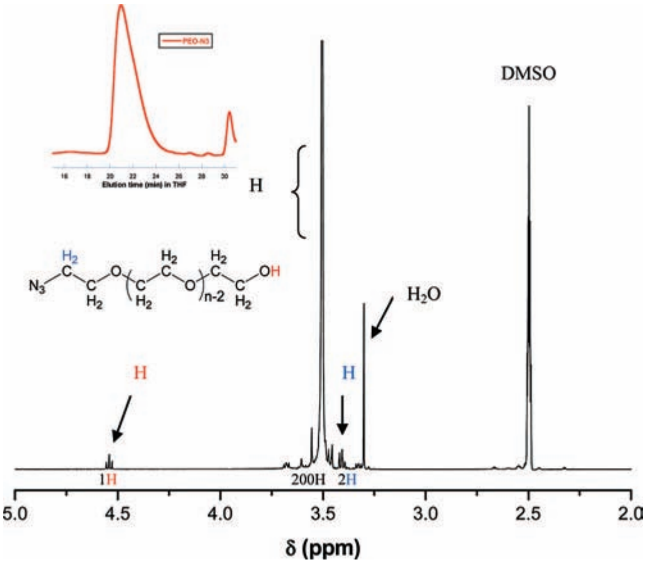

Figure 6. ^{1}H NMR spectrum and SEC trace (RI detection on top left) of α-azido,*ω*-hydroxyl PEO (entry 7, Table 1).

evidence for cyclic structures is observed. This allows us to conclude that ZROP of EO occurs under living conditions with no termination reactions due to the neutralization of the *ω*-growing chains by α-imidazolium cations and that the difunctionalization reactions attempted are all highly selective and quantitative.

The success met at synthesizing various α,*ω*-functionalized PEOs using NHC **1** as organic initiator prompted us to exploit the chemistry of NHC for the preparation of block copolymers. Use of NHC as organic catalysts only, and not as true organic initiators, has been considered so far in the context of block copolymers synthesis. Hedrick and co-workers previously showed that aliphatic block copolyesters can be derived by NHC-catalyzed ROP,[38−47] and our group also reported on the synthesis of all acrylic block copolymers by group transfer polymerization using NHCs as catalysts.[55] Our aim here is to directly grow a poly(*ε*-caprolactone) (PCL) block from a ZROP-derived PEO precursor generated by NHC **1** and thus obtain a PEO-*b*-PCL diblock copolymer in one-pot. Investigations to obtain such block copolymers have been the subject of intensive research for many years,[74−80] owing to their potential applica-

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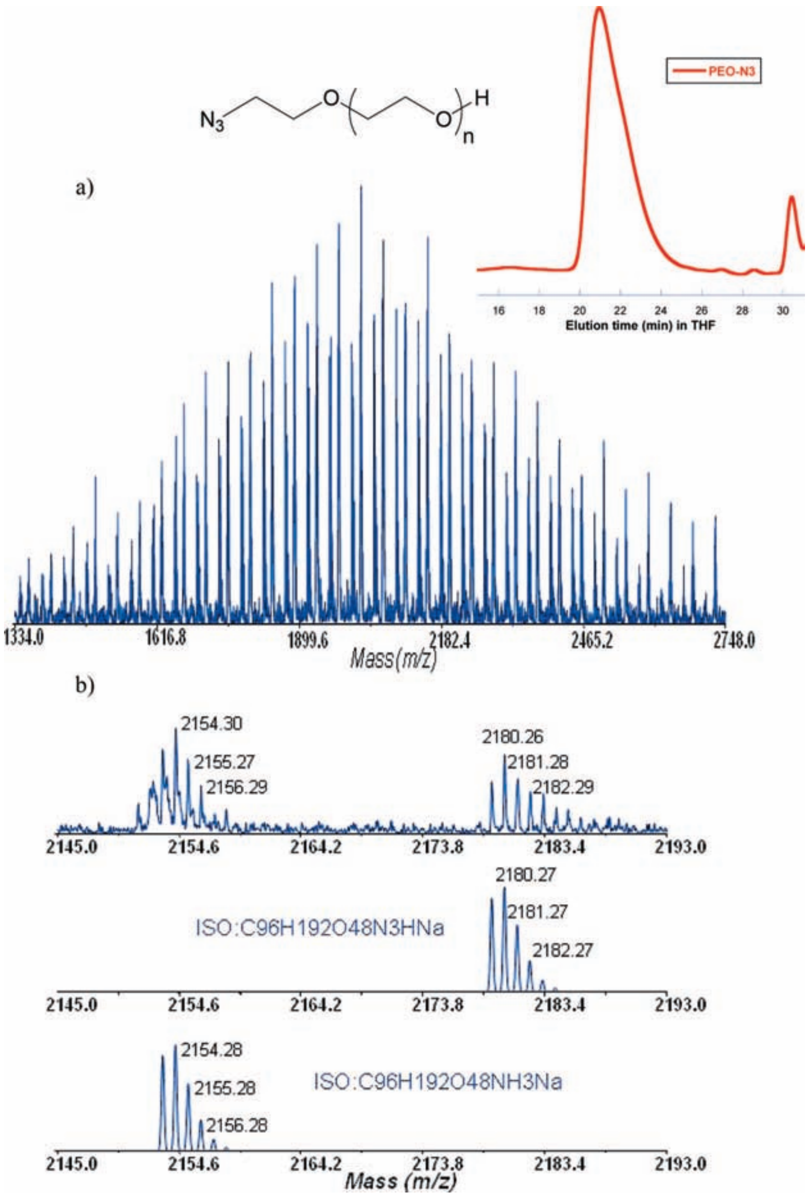

Figure 7. MALDI-TOF mass spectrum and SEC trace (RI detection on top right) of α-azido,ω-hydroxy PEO (entry 7, Table 1).

tions in the biomedical field.[81−83] Their synthesis most often requires a multistep procedure, involving the ROP of EO from an alkali metal-based initiator followed by a deactivation step to generate an OH-terminated PEO, which is subsequently used to initiate ROP of CL, with the help of a metal-based activator (e.g., stannous octoate[84] or aluminum derivatives).[75,85] In our case, CL was added onto the DMSO solution of a preformed PEO initiated by NHC **1**, without isolating that precursor (except an aliquot for SEC characterization). The reaction medium was

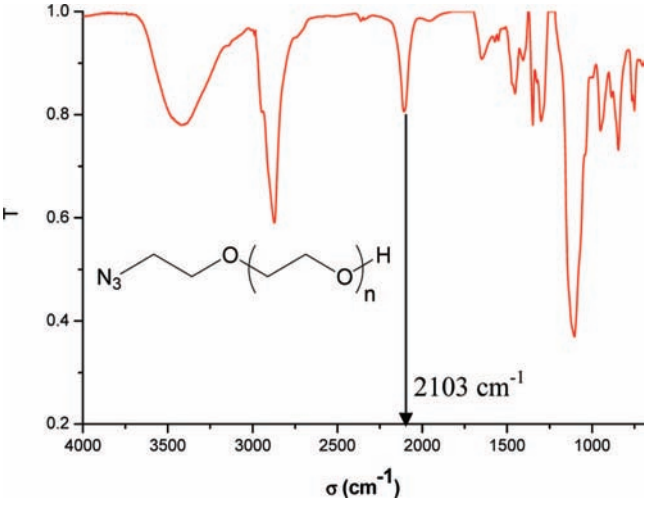

Figure 8. IR spectrum of α-azido,ω-hydroxy PEO (entry 7, Table 1).

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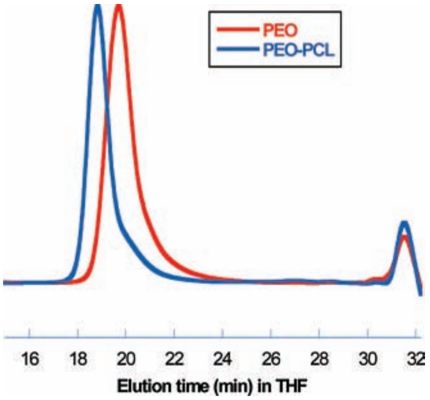

Figure 9. SEC traces (RI detection) of PEO-*b*-PCL (blue) diblock copolymer obtained from initiator NHC **1** (entry 8, Table 1) and α,ω-bis(hydroxy) PEO precursor (red).

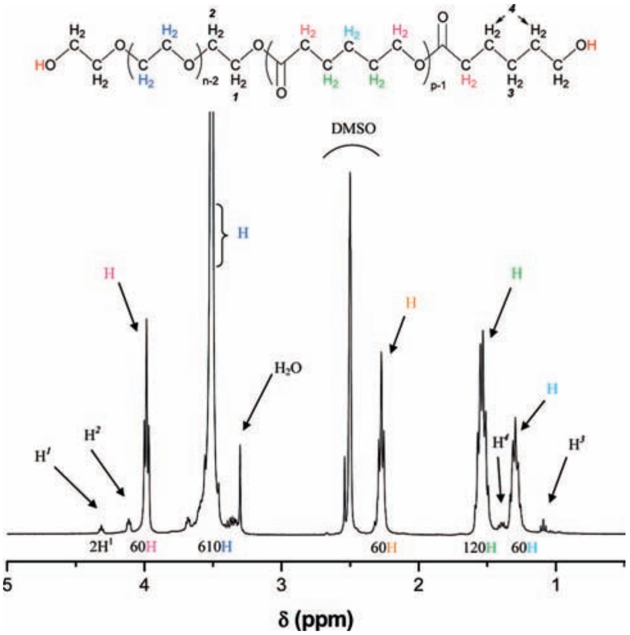

Figure 10. ^1H NMR spectrum of PEO-*b*-PCL diblock copolymer obtained from initiator NHC **1** (entry 8, Table 1).

stirred for 15 h and kept at 50 °C for the polymerization to proceed. The sample isolated was characterized by SEC whose trace shows a clear shift toward the higher molar mass domain after polymerization of CL, while polydispersity remains quite low, attesting to an effective crossover (Figure 9). Analysis by ^1H NMR confirmed the presence of both PEO and PCL blocks. Knowing accurately the molar mass of the PEO precursor, the overall composition could be calculated from the relative integrations of the characteristic peaks of both blocks (e.g., that at 3.5 ppm and that at 1.25, 1.5, 2.25, and 4 ppm) for PEO and PCL blocks, respectively. Taking the proton H^1 appearing at 4.3 ppm that is characteristic of the link between the two blocks, values of 6700 and 3400 g/mol could be deduced for the PEO and the PCL blocks, respectively, which makes a total molar mass of 10 100 g/mol for the PEO-*b*-PCL diblock copolymer (Figure 10). This latter value is in relative good agreement with the theoretical one at 50% monomer conversion, assuming that ROP of CL underwent a living/controlled path. The inference from this result is that a PEO-based imidazolium alkoxide is capable of growing a well-defined PCL block. Synthesis of other types of block copolymers based on sequential zwitterionic polymerization is currently under investigation.

Conclusions

We investigated a novel and easy synthetic route to α,ω-difunctionalized PEOs, combining significant advantages, among which prevention of metallic initiators and residues, use of commercially available terminating agents, perfect control over molar masses and polydispersities, absence of intermediate steps, and straightforward purification by precipitation. This could be achieved by using NHC as an efficient initiator for the metal-free polymerization of ethylene oxide at 50 °C in DMSO as solvent. Linear PEOs exhibiting narrow molar mass distributions can be obtained straightforwardly, and chain lengths are solely controlled by the monomer to the NHC molar ratio. The growth of these PEO chains thus occurs under living conditions with no side reaction, very likely by a ZROP mechanism. Work is in progress to evidence the presence of zwitterionic intermediate species. Through an appropriate choice of functional terminating agents of general structure NuH or $NuSiMe_3$, a variety of α,ω-difunctionalized PEOs can be derived by displacement of the imidazolium moiety by Nu. In particular, bis(hydroxy)-PEO telechelics and α-azido,ω-hydroxy-PEO heterotelechelics can be easily prepared using bifunctional terminating agents (H_2O and N_3SiMe_3, respectively). Analytical techniques such as ^1H NMR spectroscopy, SEC, and most of all MALDI-TOF mass spectrometry were used in combination to prove the absence of any cyclic species that might have resulted from an intramolecular deactivation of growing alkoxides by the imidazolium cation on the one hand, and the quantitative functionalization of PEO chain ends on the other. A well-defined poly(ethylene oxide)-*b*-poly(ε-caprolactone) block copolymer could also be directly synthesized by sequential polymerization using the same NHC as organic initiator, without isolation of the PEO block intermediate. Further studies are underway to synthesize other α,ω-difunctionalized PEOs from various NHCs and to examine the potential of the latter organic initiators for the synthesis of various block copolymers.

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