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N-Heterocyclic Carbene-Organocatalyzed Ring-Opening Polymerization of Ethylene Oxide in the Presence of Alcohols or Trimethylsilyl Nucleophiles as Chain Moderators for the Synthesis of α,ω-Heterodifunctionalized Poly(ethylene oxide)s

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ABSTRACT: The present study describes innovations in the ring-opening polymerization (ROP) of ethylene oxide (EO) using *N*-heterocyclic carbenes (NHCs) as organocatalysts, which enables the synthesis of α,ω-heterodifunctionalized poly(ethylene oxide)s (PEOs). Two representative NHC catalysts, namely, 1,3-bis(diisopropyl)imidazol-2-ylidene (**1**) and 1,3-bis(di-*tert*-butyl)imidazol-2-ylidene (**2**), were efficiently employed in conjunction with a variety of chain regulators of general structure NuE, where Nu and E are the nucleophilic and the electrophilic part, respectively, with E = H or $SiMe_3$ (e.g., $PhCH_2OH$, $HC{\equiv}CCH_2OH$, N_3SiMe_3, and $PhCH_2OSiMe_3$). Catalytic amounts of the NHC (typically [NHC]/[NuE]/[EO] = 0.1/1/100 in moles) were indeed utilized to trigger the metal-free ROP of EO at 50 °C in dimethyl sulfoxide, allowing the polymerization to proceed to completion. In this way, PEOs of dispersities lower than 1.2 and molar masses perfectly matching the [EO]/[NuE] ratio were obtained, attesting to the controlled/living character of these NHC-catalyzed polymerizations. Characterization of α,ω-difunctionalized PEOs by combined techniques such as ^{1}H NMR spectroscopy, MALDI-TOF mass spectrometry, and size exclusion chromatography confirmed the quantitative introduction of the nucleophilic moiety (Nu) and its electrophilic component (E = H or $SiMe_3$) in the α- and ω-position of the PEO chains, respectively, and the formation of polymers with narrowly distributed molar masses. These results are discussed in the light of the existence of two possible mechanisms. The first one involves a direct attack of the NHC catalyst onto EO and the formation of a zwitterionic intermediate (activated monomer mechanism). The second possibility is the activation by the NHC of the E moiety of the NuE chain regulator first and then of the α-Nu,ω-OE PEO chain (activated chain end mechanism).

Introduction

Since Bertrand et al.[1] and Arduengo et al.[2] have described the first stable carbenes in the 1990s, carbene chemistry has received a considerable attention in molecular synthesis[3−12] and more recently in macromolecular chemistry as well.[7,13−21] This discovery has familiarized stable carbenes to chemists for their application not only as versatile ligands of transition metallic complexes[22−32] but also as organocatalysts of various reactions in organic chemistry.[3] In particular, N-heterocyclic carbenes (NHCs) represent a special class of carbenes that have emerged as powerful organocatalysts.[6,33−35] The enormous catalytic potential of NHCs for a wide range of elementary reactions is due to their structural diversity and their rates and selectivities that compete with the most active and selective metal-based or enzymatic catalysts.[6,7] Many of such NHC-catalyzed reactions are based on the activation of the carbonyl group (e.g., benzoin condensation, Stetter reaction, transesterification, etc.),[4,6,36−39] though other electrophilic groups such as trimethylsilyl (TMS) ones can be activated, for instance for cyanosilylation or trifluoromethylsilylation reactions.[40−43]

To date, the potential of NHCs has been slightly exploited in organocatalyzed polymerization reactions. Yet, organocatalysis offers a reliable alternative to metal-mediated catalysis for polymer synthesis. In recent years, a few research groups, mainly Hedrick, Waymouth et al., and our group as well, have used NHCs to trigger metal-free polymerization reactions, including group transfer and ring-opening polymerizations.[7,13−21] On the basis of an activation of the carbonyl moiety, Waymouth and Hedrick et al. have developed the NHC-induced ring-opening polymerization (ROP) of cyclic esters, mainly ε-caprolactone and lactide, to produce linear as well as cyclic aliphatic polyesters.[7,13,16−18] Baceiredo et al. have taken advantage of the activation by NHC of TMS-containing reagents to catalyze the ROP of cyclosiloxanes.[44] Hedrick, Waymouth et al., and our group have also shown that silyl ketene acetals can be activated by NHCs and initiate the "controlled/living" polymerization of both methacrylic and acrylic monomers, which refers to as group transfer polymerization (GTP).[14,15,21,45]

Beyond one particular polymerization method, our ambition is to provide a single class of catalysts that could trigger various polymerization reactions for metal-free polymer synthesis. We thus aim to develop a multitask organocatalytic platform, targeting several types of polymers from one generic family of NHCs. In a recent addition to GTP, we have demonstrated that NHCs can lead to poly(l,4-phenylene-l-oxo-2-hydroxyethylene) referred to as polybenzoin, by catalyzing the step growth polymerization of terephtaldehyde.[19] Besides, we have reported that

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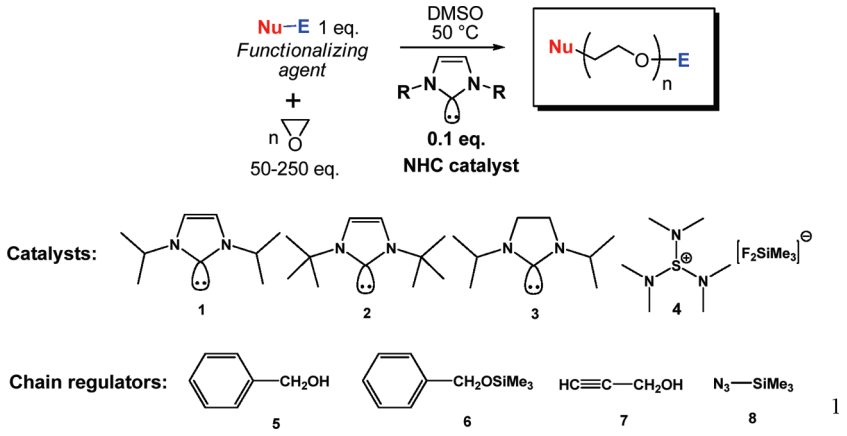


Figure 1. Ring-opening polymerization of ethylene oxide catalyzed by *N*-heterocyclic carbenes in the presence of OH- or Me_3Si-containing chain regulators (**3** and **4** were used for comparison).

1,3-bis(diisopropyl)imidazol-2-ylidene can directly initiate the metal-free ROP of ethylene oxide (EO). Addition of OH- or TMS-containing difunctional terminators at the completion of these polymerizations leads to α,ω-difunctionalized poly(ethylene oxide)s (PEOs).[20,46] In the latter case, the polymerization proceeds via the formation of a zwitterionic imidazolium alkoxide intermediate; this process has been named ZROP for zwitterionic ring-opening polymerization (ZROP).[20] Without any other reagent added at the beginning of ZROP, the PEO chain length is strictly controlled by the EO to the NHC molar ratio: typically, [EO]/[NHC **1**] = 100/1.

Here, we propose an innovation with regards to our previous works by employing NHCs as real organocatalysts in conjunction with hydroxylated or trimethylsilylated reagents introduced at the beginning and playing the role of chain regulators during ROP of EO. It has to be mentioned that Waymouth and Hedrick et al. have briefly reported in a proceeding that ROP of EO can be triggered by a NHC in the presence of an alcohol as initiator.[47] Here we demonstrate that NHCs **1** or **2** can catalyze the metal-free ROP of EO in the presence of a variety of chain regulators of NuE type, where Nu and E are the nucleophilic and the electrophilic part, respectively, with E = H or $SiMe_3$ (Figure 1). In this way, α,ω-difunctionalized PEOs become accessible in a versatile fashion combining excellent control of molar masses, narrow dispersities, quantitative chain-end functionalization, and absence of metallic residues.

PEO, also referred to as poly(ethylene glycol) (PEG), has been extensively utilized in the biomedical field owing to its chemical stability, its solubility in both organic and aqueous media, its nontoxicity, its low immunogenicity, and antigenicity.[48] Biomedical applications of PEO often require α,ω-difunctional PEO oligomers possessing reactive end functions.[49−60] However, straightforward synthetic pathways to such heterodifunctional PEOs that meet different criteria such as control over molar masses and dispersities, mild reaction conditions, and PEO chain-end functionalization are not that common. Most importantly, the removal of metallic contaminants generally introduced by the initiator is a necessity in biomedical applications involving PEO. In this regard, the organocatalyzed synthetic pathway to functionalized PEOs that is proposed here appears as a promising methodology offering all the aforementioned advantages.

Experimental Section

Materials. Ethylene oxide (EO) (Fluka, 99.8%) was distilled over sodium into a buret. All other reagents were purchased from Aldrich. Dimethyl sulfoxide (DMSO) was dried over CaH_2 during several days and distilled prior to use following a minimum of 5 h reflux. Tetrahydrofuran (THF) was distilled over sodium/benzophenone to prepare solutions of the NHCs **1** and **2**. Benzyl alcohol (**5**) and propargyl alcohol (**7**) were distilled and stored over molecular sieves. Benzyl trimethylsilyl ether (**6**) was prepared by silylation of benzyl alcohol using hexamethyldisilazane and trimethylsilyl chloride and purified by fractionated distillation. Trimethylsilyl azide (**8**) was dried and distilled over CaH_2. Tris(dimethylamino)sulfonium bifluorotrimethylsilicate ($TASF_2SiMe_3$, **4**) was purchased from Aldrich (technical grade) and used as received. NHCs **1** and **2** were prepared by slightly modifying already reported procedures:[61] the diisopropylimidazolium salt (purity ≥97%) was deprotonated with NaH and a catalytic amount of tBuOK. NHC **1** was purified by distillation under vacuum. As for the di-*tert*-butylimidazolium salt (purity ≥98%), it was deprotonated with nBu-Li, affording NHC **2** which was purified by sublimation under vacuum. Solutions of these catalysts were kept in a glovebox under an argon atmosphere.

Synthesis of NHC 3. A 150 mL round-bottom flask equipped with a stir bar was charged with 2.0 g (10.5 mmol) of 1,3-diisopropylimidazolium chloride, potassium *tert*-butoxide (90 mg, 0.8 mmol), and sodium hydride (600 mg, 15 mmol) used as a 60 wt % dispersion in silicon oil. 20 mL of freshly distilled THF was added dropwise to the above suspension. The mixture was stirred for 5 h at RT and filtrated under vacuum using a fritted glass filter, porosity G5. Volatiles were removed under vacuum, and the obtained pale viscous liquid was distilled under vacuum to provide NHC **3** as a clear liquid (1.3 g, 80% yield). ^{1}H NMR (THF-d_8): δ 1.5 (s, CH_3, 12 H), 4.5 (m, CH(CH_3)$_2$, 2 H), 3.65 (s, NCH_2C, 4 H). ^{13}C NMR: δ 25 (s, *C*H$_3$), 54 (s, *C*H−(CH$_3$)$_2$), 51 (s, N*C*H$_2$C), 236.8 (s, N*C*N).

Synthesis of α,ω-Difunctionalized Poly(ethylene oxide)s. Ring-opening polymerization of EO was carried out under a dry and inert atmosphere using Schlenk equipments. In a typical polymerization, 75 μL of a 1 M solution of NHC **1** or **2** (7.5×10^{-5} mol) and 100 μL of N_3−$SiMe_3$ (7.5×10^{-4} mol) (entry 1, Table 1) were introduced with syringes in a vacuumed flame-dried Schlenk kept in a glovebox under an argon atmosphere. After removal of the Schlenk from the glovebox, 20 mL of dry DMSO was added under nitrogen. After homogenization, 2 mL (4×10^{-2} mol) of EO was introduced at −20 °C. The Schlenk was allowed to warm up to room temperature and set in a thermostated oil bath at 50 °C for 4 days. After a couple of minutes, the color turned orange to bright red (depending on the chain regulator, silylated ones giving deeper colors). Few drops of a degassed MeOH/HCl mixture were then introduced to quench the reaction. The color turned pale yellow, and the reaction mixture was allowed to stir for several minutes. The DMSO solution was precipitated in a large excess of diethyl ether at room temperature. The polymer was redissolved in dichloromethane, precipitated twice in diethyl ether, and recovered as a white powder that was

Table 1. NHC-Catalyzed Ring-Opening Polymerization of Ethylene Oxide in DMSO at 50 °C in Presence of a Functionalizing Chain Regulator of NuE Type[a]

exp	CR[b]	NHC	[NHC]/[CR]/[M][f]	conv (%)	$M_{n,theo}$[c]	$M_{n,SEC}$[d]/ $M_{n,NMR}$[e]	D[d]
1	$PhCH_2OH$	**1**	0.1/1/43	100	2000	1900/2000	1.15
2	$PhCH_2OSiMe_3$	**1**	0.1/1/36	100	1800	1700/1900	1.12
3	$PhCH_2OSiMe_3$	**1**	0.1/1/240	95	10000	10600/12100	1.1
4	$PhCH_2OSiMe_3$	**2**	0.1/1/36	100	1800	1600/1800	1.14
5	$HC{\equiv}CCH_2OH$	**1**	0.1/1/44	100	2000	2100/2200	1.1
6	$HC{\equiv}CCH_2OH$	**2**	0.1/1/44	95	1900	2000/2100	1.1
7	$N_3{-}SiMe_3$	**1**	0.1/1/53	100	2400	2300/2500	1.07
8	$N_3{-}SiMe_3$	**1**	0.1/1/133	95	5600	5400/5800	1.06
9	$N_3{-}SiMe_3$	**1**	0.1/1/265	90	10500	10200/12000	1.09
10	$N_3{-}SiMe_3$	**2**	0.1/1/53	100	2400	2200/2300	1.08

[a] Attempts to polymerize EO using either NHC **3** or $TASF_2SiMe_3$ (**4**) as catalyst did not give any polymer (see text). [b] Functionalizing chain regulator. [c] Theoretical molar mass: $M_{n,theo}$ = ([monomer]/[CR]) × conv × M_{EO} + M_{CR}, where M_{EO} and M_{CR} are the molar masses of the monomer unit and the chain regulator (CR), and conv is the conversion of EO determined by gravimetry. [d] Experimental molar masses and disperisty index (D) obtained by SEC in THF using PEO standards for calibration. [e] Experimental molar masses determined by ^1H NMR using characteristic peaks as references for integration (see text). [f] [NHC]/[CR]/[M] represents the initial molar ratio of the components.

dried under vacuum. Molecular characteristics of all NHC-derived PEOs are provided in Table 1.

Synthesis of α-N_3,ω-OH-Functionalized PEO. M_n = 2300 g/mol by SEC; PDI = 1.07. ^1H ($CDCl_3$): 3.6 ppm (CH_2O-), 3.4 ppm ($N_3-CH_2CH_2O$). ^{13}C ($CDCl_3$): 70.6 ppm (CH_2O-), 50.9 ppm ($N_3-CH_2CH_2O$), 72.7 ppm ($-OCH_2CH_2OH$), and 61.8 ppm ($-OCH_2CH_2OH$).

Synthesis of α-$C_6H_5CH_2O$,ω-OH-Functionalized PEO (or ω-$OSiMe_3$ before Hydrolysis). M_n = 1700 g/mol by SEC; PDI = 1.12. ^1H (DMSO-d_6): 3.6 ppm (CH_2O-), 7.3 ppm ($C_6H_5-CH_2O$), 4.5 ppm ($C_6H_5-CH_2O$) and 4.55 ppm ($-OCH_2CH_2OH$) (or 0 ppm ($-OCH_2CH_2OSi(CH_3)_3$)).

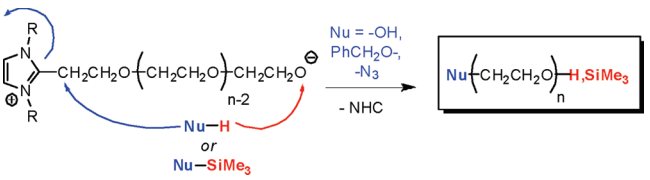
Synthesis of α-Propargyl,ω-OH-Functionalized PEO. M_n = 2100 g/mol by SEC; PDI = 1.1. ^1H ($CDCl_3$): 3.6 ppm (CH_2O-), 4.2 ppm ($HC{\equiv}C-CH_2O-$) and 2.4 ppm ($HC{\equiv}C-CH_2O-$) J_4 coupling = 2 Hz. ^{13}C ($CDCl_3$): 70.6 ppm (CH_2O-), 79.7 ppm ($HC{\equiv}C-CH_2O-$), 74.7 ppm ($HC{\equiv}C-CH_2O-$), 58.5 ppm ($HC{\equiv}C-CH_2O-$), 69.3 ppm ($HC{\equiv}C-CH_2O-CH_2-$), 72.7 ppm ($-OCH_2CH_2OH$), and 61.9 ppm ($-OCH_2CH_2OH$).

Characterization. ^1H NMR spectra were recorded on a Bruker AC 400 spectrometer. Molar masses of PEO samples were determined by size exclusion chromatography (SEC) that was performed using a three-column set of TSK gel TOSOH (G4000, G3000, and G2000 with pore sizes of 20, 75, and 200 Å, respectively, connected in series) calibrated with PEO standards with THF as eluent (1 mL/min) and trichlorobenzene as a flow marker at 25 °C, and using both refractometric and UV detectors (Varian). 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 1000 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 (ATR) method from films obtained with CH_2Cl_2 as solvent.

Results and Discussion

In a previous contribution,[20] we have demonstrated that NHC **1** can initiate by itself the zwitterionic ring-opening polymerization (ZROP) of EO. The growing species, namely 1,3-bis-(diisopropyl)imidazol-2-ylidinium alkoxide, were quenched at the completion of ZROP by a functionalizing terminator of

Scheme 1. Functionalizing Terminators of the Zwitterionic Ring-Opening Polymerization of Ethylene Oxide[20]



NuH or $NuSiMe_3$-type, leading to α-Nu,ω-OH (or α-Nu,ω-$OSiMe_3$)-difunctionalized PEOs. The quantitative introduction of the Nu moiety in the α-position and of OH (or $OSiMe_3$) in the ω-position of PEO chains occurred through the nucleophilic substitution of the imidazolium moiety by $Nu^{\delta-}$ and the concomitant reaction of the ω-growing alkoxide of PEO chain with $H^{\delta+}$ (or $Me_3Si^{\delta+}$), as illustrated in Scheme 1.

Here we investigate the ROP of EO with NHCs not used as initiators but as real organocatalysts, in conjunction with functionalizing reagents of NuE-type as chain regulators (with E = H or $SiMe_3$, Figure 1). All ingredients were thus introduced at the early stage of the polymerization, with typical amounts of NHC catalyst equal to 10 mol % relative to NuE (Table 1). As previously reported,[20] NHC **1** or NHC **2**, namely, 1,3-bis-(diisopropyl)imidazol-2-ylidene and 1,3-bis(di-*tert*-butyl)imidazol-2-ylidene, respectively, are catalysts of choice as for their ease of purification by distillation or by sublimation, affording "bare catalysts" free of any metallic residues. Handling such bare NHCs was preferred over generating NHCs *in situ* by deprotonation of corresponding imidazolium-based ionic liquids with a strong base (e.g., *t*BuOK, NaH, or BuLi).[20] Indeed, this might have interfered with the ROP of EO and introduced undesirable metallic contaminants in the resulting PEOs.

NHC **3** and tris(dimethylamino)sulfonium bifluorotrimethylsiliconate, known as $TASF_2SiMe_3$, **4**, have also been tested to catalyze ROP of EO under the same conditions used with **1** and **2** as catalysts. NHC **3**, 1,3-bis(diisopropyl)imidazolin-2-ylidene, which can also be obtained pure by distillation is more nucleophilic than NHCs **1** and **2**, which is related to the absence of the unsaturation in the five-member ring (saturated NHC).[62] $TASF_2SiMe_3$ is a common catalyst of GTP of methacrylic monomers and is capable of activating the O−Si bond of silyl ketene acetals. It has also been reported that $TASF_2SiMe_3$ can cleave silylated ethers, generating transient alkoxides.[63−66]

Four representative NuE-type chain regulators were investigated in this work (Figure 1): two O−H and two TMS-containing reagents. Trimethylsilyl nucleophiles (Me_3SiNu) have long been recognized as effective alternatives of proton nucleophiles (HNu) in addition reactions onto various electrophiles such as aldehydes,

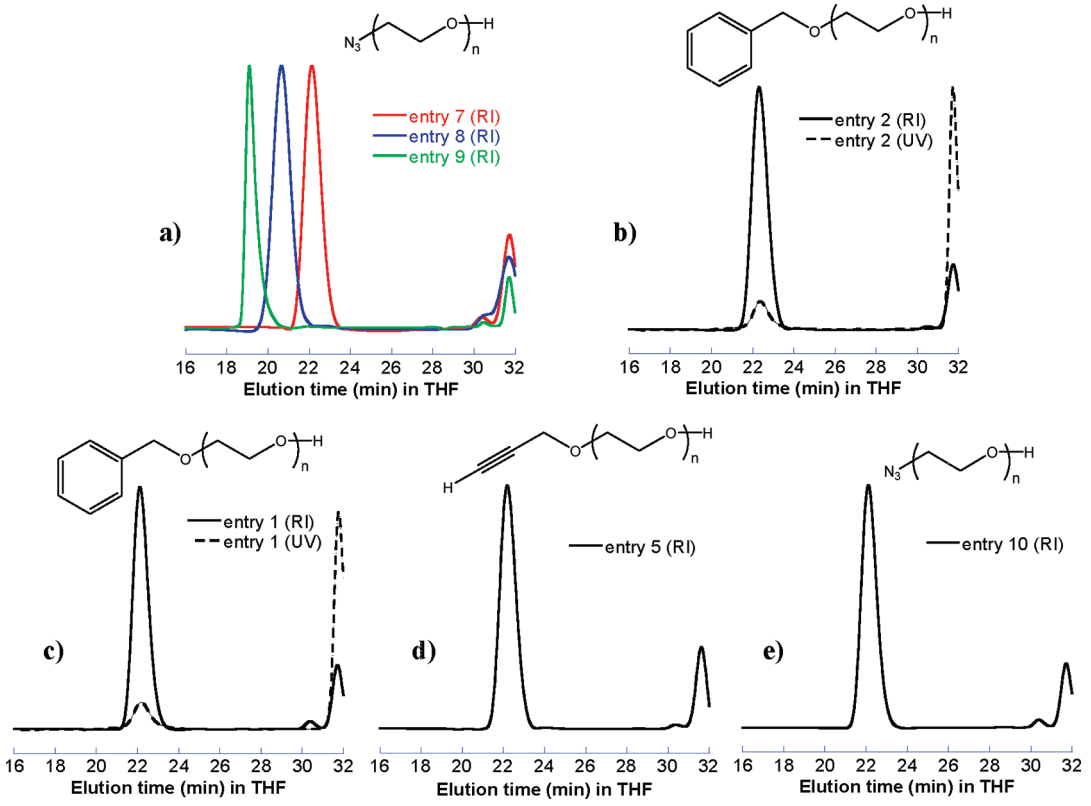


Figure 2. SEC traces (refractive index (RI) and UV detectors) of poly(ethylene oxide) synthesized from chain regulator: (a) N_3SiMe_3, (b) $PhCH_2OSiMe_3$, (c) $PhCH_2OH$, (d) $HC{\equiv}CCH_2OH$, and (e) N_3SiMe_3. From (a) to (d), NHC **1** was used as catalyst while for (e) NHC **2** was used.

ketones, imines, oxiranes, aziridines, and nitrones, among others.[67] Both benzyl alcohol ($PhCH_2OH$, **5**) and benzyl trimethylsilyl ether ($PhCH_2OSiMe_3$, **6**) were selected because the benzyl group (Bz) that is expectedly introduced in α-position of PEO chains can be easily revealed by ^1H NMR as well as by UV spectroscopy. As for propargyl alcohol ($HC{\equiv}CCH_2OH$, **7**) and trimethylsilyl azide (N_3SiMe_3, **8**), such functional chain regulators directly introduce an alkyne and an azido group, respectively, in the α-position of PEO chains. Organic azides and alkynes have recently received considerable attention owing to their ability to undergo the Huisgen 1,3-dipolar cycloaddition ("click chemistry"), a versatile method of creating C−C (or C−N) bonds under mild experimental conditions, combining tolerance of functional groups and high yields.[48,68−77] However, little attention has been paid to versatile synthetic methods to azido- or alkyne-terminated PEOs.[48,56]

In a typical polymerization experiment utilizing NHC **1** as catalyst and **5** as chain regulator, we first observed that almost no polymer was formed when using THF as solvent at room temperature for overnight. In contrast, near-quantitative yields were obtained by carrying out the ROP of EO at 50 °C in DMSO (Table 1). After several minutes of reaction, the color of the solution turned from slightly orange to deep red (depending on the chain regulator, silylated ones giving deeper colors); the color tended to deepen further in the course of the reaction. After work-up, the molar masses of the obtained PEOs were found to coincide with the targeted values based on the initial [EO]/[NuE] molar ratios, with dispersities (*Đ*s) lower than 1.2. In addition, very high end-group fidelity was noted; i.e., both the Nu moiety and the H (or $SiMe_3$) group were incorporated onto every PEO chain (see further). The ROP of EO catalyzed by NHC thus exhibit features of a "controlled/living" process over a range of molar masses, from 1800 to 12 100 g/mol (Table 1). This range is typical for the PEO derivatives used for PEGylation reactions in biomedical applications.[48]

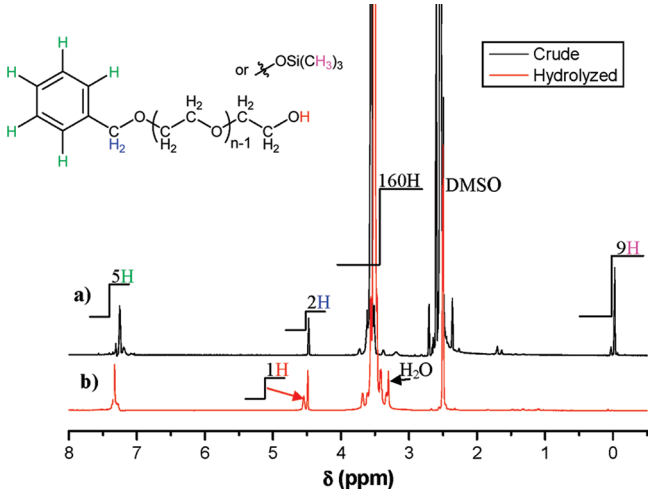


Figure 3. ^1H NMR spectrum in DMSO-d_6 of (a) α-benzyl,ω-trimethylsilyloxy heterodifunctional poly(ethylene oxide) (PEO) before adding methanol and of (b) α-benzyl,ω-hydroxy heterodifunctional PEO (entry 2, Table 1) obtained after treatment by methanol.

Figure 2 shows that all PEO derivatives exhibit symmetrical and monomodal size exclusion chromatography (SEC) traces, with experimental molar masses in close agreement with the theoretical values. In particular, the UV signal detector operating at 254 nm that is specific to the absorption of aromatic groups (EO units do not absorb at this wavelength) reveal the presence of the benzyl groups of both PEO samples synthesized from benzyl-containing chain regulators **5** and **6**.

Both OH and TMS nucleophiles can thus be used as chain regulators of ROP of EO catalyzed by imidazol-2-ylidenes (NHCs **1** and **2**), by controlling the molar mass of the PEOs. In contrast, 1,3-bis(diisopropyl)imidazolin-2-ylidene (NHC **3**) and

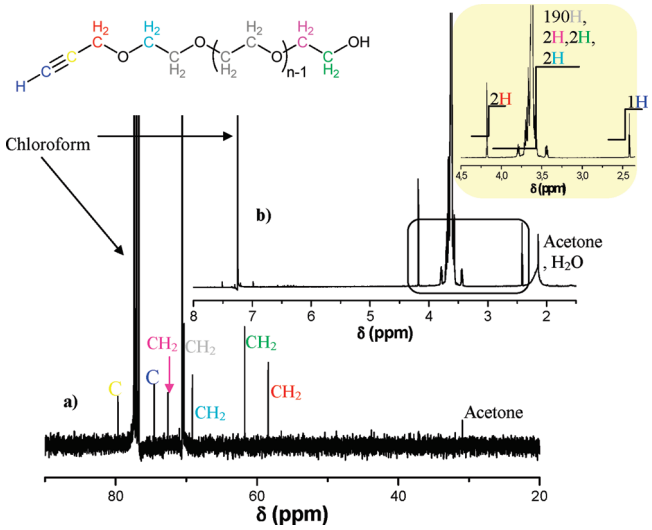


Figure 4. ^{13}C NMR (a) and ^{1}H NMR (b) spectrum in $CDCl_3$ of α-propargyl,ω-hydroxyl heterodifunctional poly(ethylene oxide) (entry 5, Table 1).

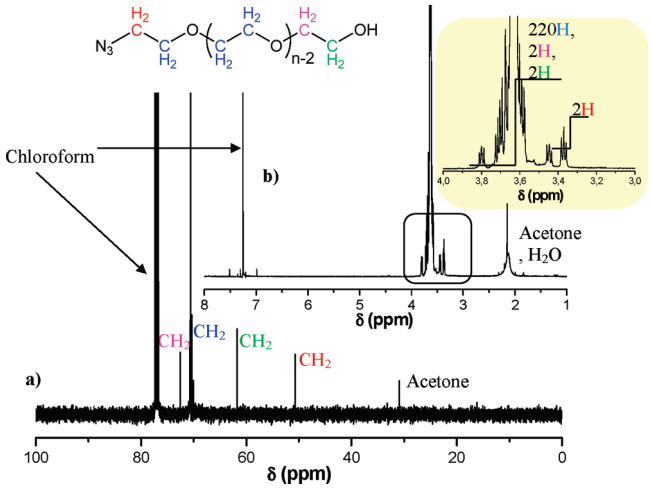


Figure 5. ^{13}C NMR (a) and ^{1}H NMR (b) spectrum in $CDCl_3$ of α-azido,ω-hydroxyl heterodifunctional poly(ethylene oxide) (entry 1, Table 1).

$TASF_2SiMe_3$ (**4**) could not trigger EO polymerization in presence of compounds **5** or **6**: under the same conditions used with NHC **1** or **2**, no polymer was obtained. Surprisingly and despite a higher nucleophilicity as compared to **1**, NHC **3** did not form either any PEO when used as direct initiator for ZROP of EO in absence of chain regulator, in contrast to NHC **1**.[20] A possible explanation for the particular behavior of NHC **3** is given further.

The molecular features of PEOs obtained from imidazol-2-ylidenes **1** or **2** were next investigated by ^{1}H and ^{13}C NMR spectroscopy and matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry. In Figure 3 are given the ^{1}H NMR spectra of the PEO sample obtained from the $PhCH_2OSiMe_3$ chain regulator and catalyzed by NHC **1** (entry 2, Table 1), before and after addition of acidic methanol (see Experimental Section). A peak corresponding to the resonance of the protons of the TMS moiety can be observed at 0 ppm before treatment with MeOH, which is consistent with the formation of a α-benzyl,ω-trimethylsilyloxy heterodifunctional PEO. After addition of MeOH, this peak vanished, and a new peak assigned to the resonance of the terminal hydroxyl proton is detected at 4.55 ppm. In addition, characteristic protons of benzyl groups are clearly identified at 7.3 ppm (C_6H_5−CH_2O) and 4.5 ppm (C_6H_5−CH_2O). The relative integration of these peaks to that characteristic of the protons of PEO chains at 3.5 ppm provides another means to determine the molar mass of these PEOs, assuming the presence of a benzyl terminal group at every PEO chain. An excellent agreement between M_n values determined by SEC (1700 g/mol) and by ^{1}H NMR (1900 g/mol) is found. The molar mass is determined by ^{1}H NMR using the following equation:

$$M_{n,PEO} = \frac{I_a M_{EO}}{2I_b} + M_{CR}$$

where I_a, I_b, M_{EO}, and M_{CR} are respectively the intensity of methylene protons a of the monomer unit (CH_2CH_2O around 3.5 ppm) and of the methylene protons b from the $-CH_2-$ adjacent to the benzyl group of **6** (in that case at 4.5 ppm), the molar mass of the EO monomer unit (44.05 g/mol), and the molar mass of chain regulator **6** (108.14 g/mol). The same formula can be applied to the various PEOs prepared since they all possess characteristic methylene groups adjacent to the Nu functionality of the chain regulator. These results indicate that both benzyl alcohol and benzyl trimethylsilyl ether can well be used to

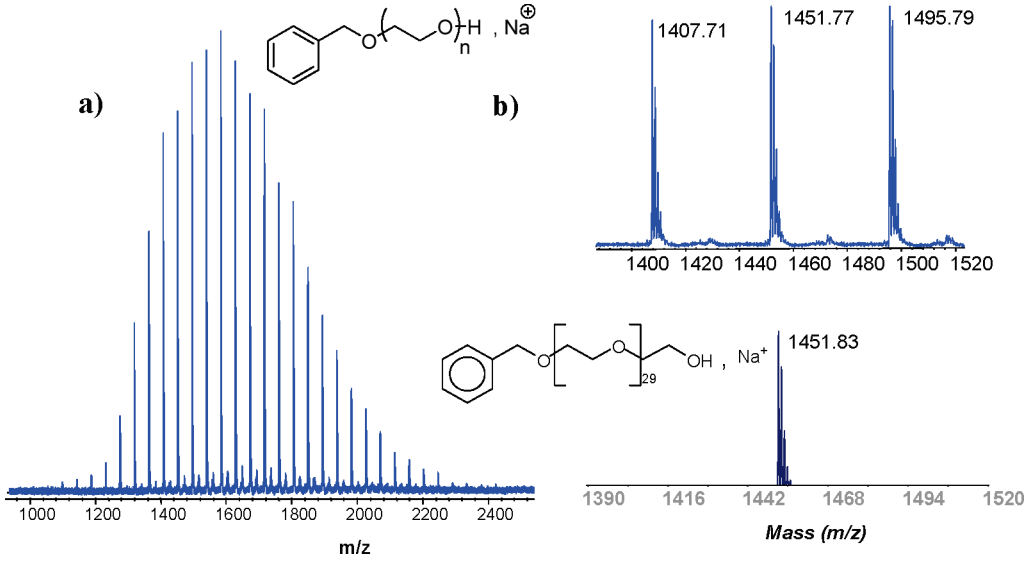


Figure 6. Experimental (a) and simulated (b) MALDI TOF MS of α-benzyl,ω-hydroxyl heterodifunctional poly(ethylene oxide) (entry 2, Table 1).

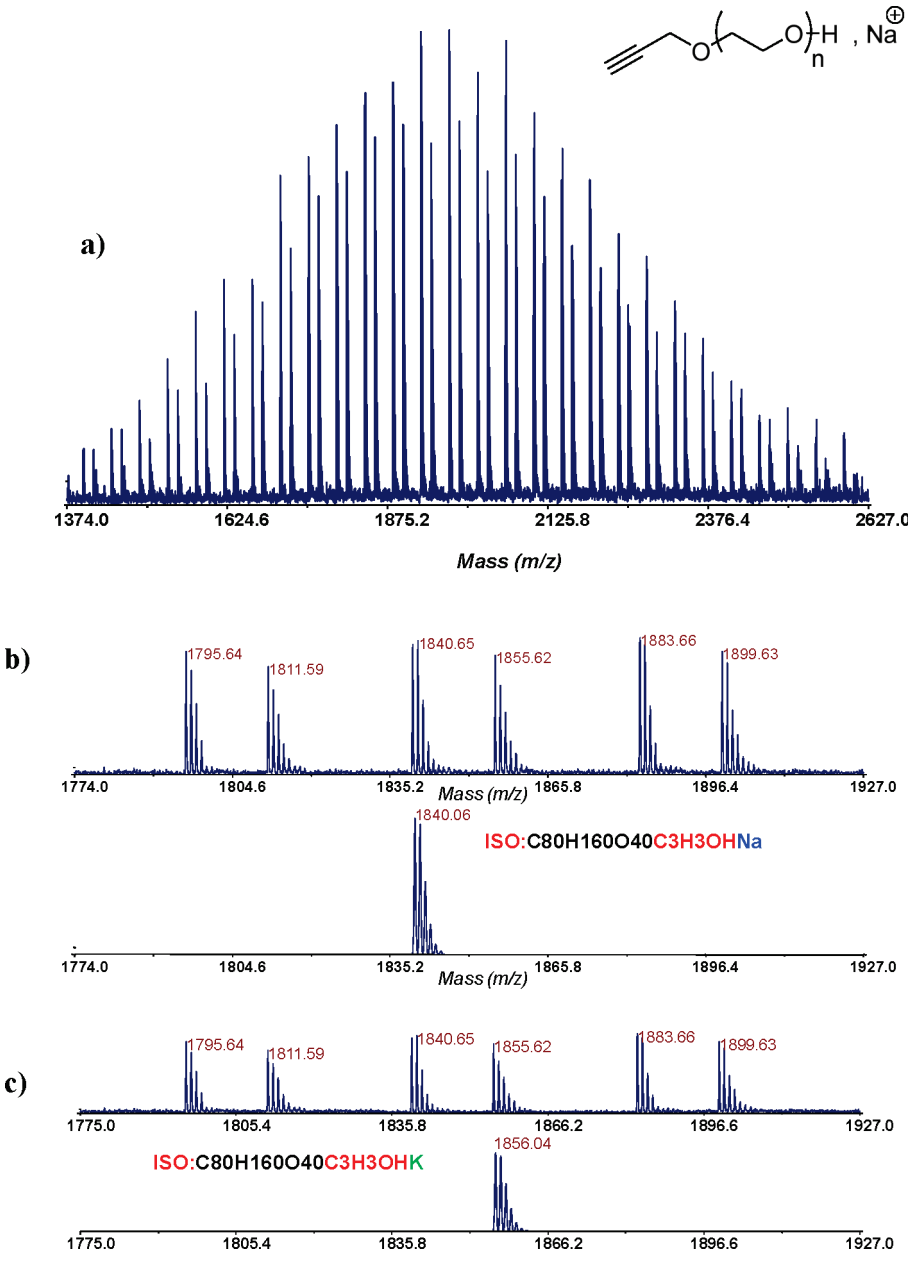


Figure 7. MALDI TOF MS of α-propargyl,ω-hydroxyl heterodifunctional poly(ethylene oxide) (entry 5, Table 1). (a) MALDI TOF spectrum using NaI as ionizing salt. (b) Comparison between experiment and simulation with the software of the expected mass (a second population can be observed). (c) Simulation of the second population: possibility of a preferential ionization with residual potassium (see also Figure 8).

mediate the metal-free ROP of EO, with no side reaction detected. This could be extended to other hydroxy- or TMS-containing reagents as a means to generate α,ω-hydroxy heterodifunctionalized PEOs following this organocatalyzed synthetic pathway.

An alkyne moiety could also be directly introduced in the α-position of PEO by mediating the ROP of EO with propargyl alcohol (**7**) which is a commercially available alcohol. The ^{1}H and ^{13}C NMR spectra of the expected α-propargyl,ω-hydroxyl heterodifunctional PEO prepared by the HC≡CCH$_2$OH-mediated, NHC **1**-catalyzed ROP of EO (entry 5, Table 1) are shown in Figure 4. The characteristic triplet at 2.4 ppm due to the resonance of the terminal alkyne proton and that at 4.2 ppm (doublet) attributable to two methylene protons adjacent to the alkyne group are both detected. In the equation mentioned above, I_b and M_{CR} are, in this case, the intensity of methylene protons b from the −CH$_2$− adjacent to the alkyne group and the molar mass of **7**. The carbons of the main chain (*C*H$_2$*C*H$_2$O−) appear at 70.6 ppm, the carbon atoms of the alkyne moiety are detected at 79.7 ppm (H*C*≡C−CH$_2$O−), and 74.7 ppm (HC≡*C*−CH$_2$O−), whereas the carbon atom of the methylene group adjacent to the alkyne (HC≡C−*C*H$_2$O−) is observed at 58.5 ppm. Finally, the following carbon atoms HC≡C−CH$_2$O−*C*H$_2$−, −OCH$_2$*C*H$_2$OH, and −O*C*H$_2$CH$_2$OH appear at 69.3, 72.7, and 61.9 ppm, respectively. Importantly, the alkyne hydrogen of chain regulator **7** does not interfere with ROP of EO, the targeted α-propargyl-ω-hydroxyl heterodifunctional PEO being eventually obtained without any loss of the terminal functional group.

Finally, Figure 5 shows both ^{1}H NMR and ^{13}C spectra of a PEO synthesized by the N_3SiMe_3-mediated, NHC **1**-catalyzed ROP of EO (entry 7, Table 1) with peak assignments. All the expected peaks are observed, in particular the triplet at 3.4 ppm in the ^{1}H NMR spectrum and the peak 50.9 ppm in the ^{13}C NMR spectrum, which are characteristic respectively of the resonance of the protons (−C*H*$_2$N$_3$) and the carbon atom (−*C*H$_2$N$_3$) of the methylene group in the α-position to the azido moiety.[56] Assuming

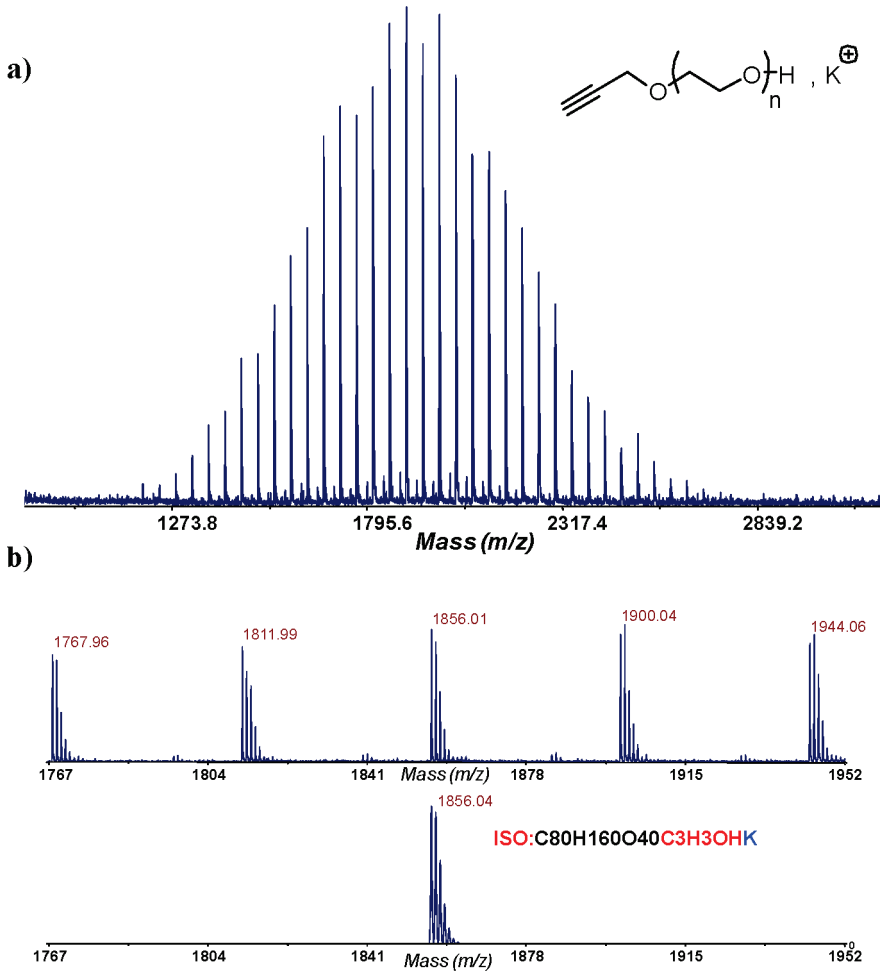


Figure 8. MALDI TOF MS of α-propargyl,ω-hydroxyl heterodifunctional poly(ethylene oxide) (entry 5, Table 1): (a) MALDI TOF spectrum using KCl as ionizing salt. (b) Comparison between experiment and simulation with the software of the expected mass with cation potassium.

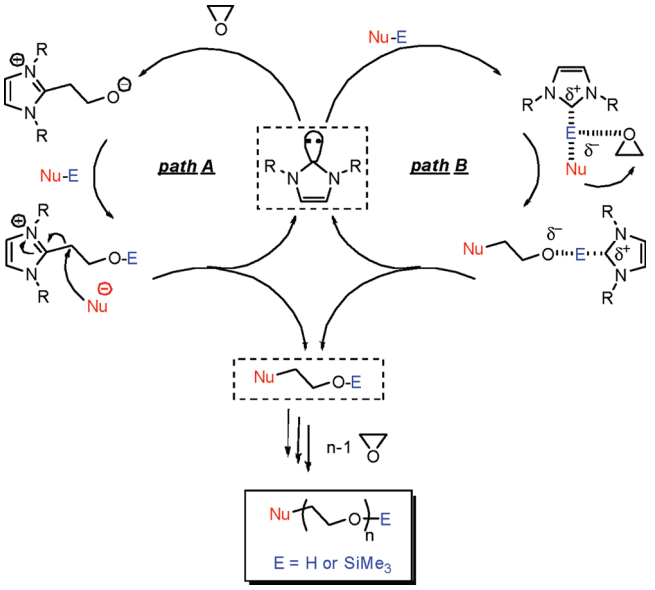
the presence of one azido terminal group at every PEO chain, the molar mass calculated using the equation previously mentioned (2500 g/mol) is again very close to the value determined by SEC (2300 g/mol) and to that predicted by the molar ratio of EO to chain regulator **3** (2400 g/mol). In the equation, I_b and M_{CR} are, this time, the intensity of methylene protons b from the $-CH_2-$ adjacent to the azido group (chain regulator **8**) and the molar mass of chain regulator **8**. The presence of the $-N_3$ moiety was also checked by IR spectroscopy, which shows a characteristic band at 2103 cm^{-1}.

Another piece of evidence that confirms the molecular structure of these PEOs and the quantitative introduction of Nu and OH groups at chain ends is provided by MALDI-TOF mass spectrometry. Figures 6−8 show representative MALDI TOF mass spectra of three selected α,ω-heterodifunctionalized PEOs. Each of the three samples analyzed shows relatively narrow molar mass distributions. In all cases, the molecular ion corresponding to the linear PEO complexed by sodium can be detected. A peak-to-peak mass increment of each population observed is equal to 44.05 g/mol, which corresponds exactly to the molar mass of one EO unit. Only one single distribution is observed for the PEO sample grown from benzyl trimethylsilyl ether (**6**) as chain regulator and eventually treated with methanol (Figure 6). The series of peaks appear at $m/z = 44.05n + M_{benzyl} + M_{OH} + 23$, where n is the degree of polymerization, 23 is the molar mass of the sodium ion generated during the ionization process, and M_{benzyl} and M_{OH} are the molar mass of a benzyl group and a hydroxyl group, respectively (M_{benzyl} = 91 and OH = 17 g/mol). Simulations giving the theoretical isotope distributions are in perfect agreement with the experimental distribution, all signals being attributed to the cationized adduct (with Na^+) of the targeted α-benzyl,ω-hydroxyl PEO.

As for the compound synthesized from N_3SiMe_3 (**8**) as chain regulator, an overlap of two distinct populations is observed (ESI). Similar observations were made in our previous report for an α-azido,ω-hydroxy difunctionalized PEO prepared by NHC-initiated ZROP.[20] However, both distributions of PEO chain can be easily accounted for. The presence of the expected population with its terminal N_3-function can be indeed clearly distinguished from a second population indicative of the loss of molecular N_2 from the former population during the ionization process.

Figure 7 pertaining to the PEO obtained by HC≡CCH_2OH (**7**)-induced ROP of EO also shows two distinct populations of peaks. One represents the targeted α-propargyl,ω-hydroxyl PEO ionized by the sodium cation, with a series of peaks appearing at $m/z = 44.05n + M_{propargyl} + M_{OH} + 23$. The second population is ascribed to a preferential ionization by the potassium cation (K^+ is always present in sodium salts, but it could also arise from the glassware during the purification process). The series of peaks appear in this case at $m/z = 44.05n + M_{propargyl} + M_{OH} + 39$, where 39 is the molar mass of the potassium ion. This was supported by using KCl as ionizing agent for analysis by MALDI TOF mass spectroscopy. As a matter of fact, only one single population perfectly matching with the simulation using K^+ cation is observed (Figure 8), with both HC≡$C-CH_2O-$ and −H coming from the propargyl alcohol used as chain regulator.

Scheme 2. Proposed Mechanisms of Initiation in Ring-Opening Polymerization of Ethylene Oxide Catalyzed by *N*-Heterocyclic Carbenes: Monomer Activation (Path A) and Chain-End Activation (Path B)

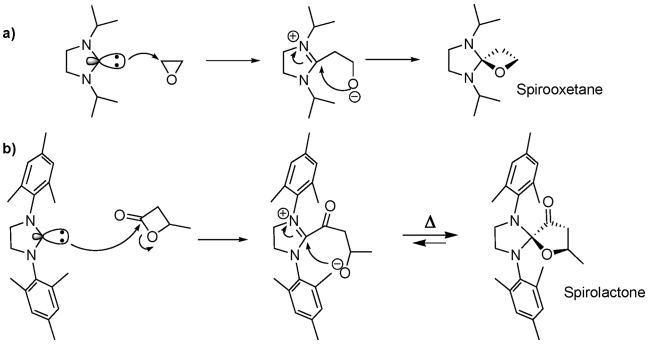


Here again, the theoretical isotope distributions are in perfect concordance with the experimental distributions. This allows us to conclude that the nonprotected alkyne functionality is preserved, not only during the course the anionic ROP of EO but also during the ionization process of the MALDI TOF analysis.

Even though the prime goal of this contribution was to investigate the conditions for the catalysis of ROP of EO by NHC, preliminary arguments can be provided here as to the mechanism that occurs in such polymerizations. Similarly to ROP of cyclic esters,[7] two distinct mechanisms of initiation and chain growth can be contemplated, depending on the interaction of the O−H or TMS-containing chain regulators with NHC catalysts against that of the latter with the monomer (Scheme 2). Indeed, NHCs are nucleophilic and silicophilic enough to activate the electrophilic part (E = H or $SiMe_3$) of NuE chain regulators.[6] Background literature clearly indicates that silylated groups are prone to activation by NHCs, a feature that has been exploited for instance in the Mukaiyama reaction or for the cyano- or the trifluorosilylation of ketones.[41−43,67,78−80] Besides, Movassaghi et al. have reported that NHCs can activate alcohols by hydrogen bonds, allowing for the NHC-catalyzed amidation of esters with amino alcohols.[81] Thus, both trimethylsilylated (**6** and **8**) and hydroxylated (**5** and **7**) chain regulators could be activated by NHCs, followed by monomer insertion as shown in path B of Scheme 2, referring to as the chain-end activation mechanism. Activation of enals by NHCs followed by ring-opening of substituted epoxides has been recently reported.[82] However, a direct nucleophilic attack by the NHC catalyst onto the monomer is also plausible (path A). We provided unambiguous evidence that NHCs can directly add onto EO in absence of any other electrophile (ZROP).[20] Protonation (or silylation) of the zwitterionic intermediate species by an alcohol (or a TMS nucleophile), followed by addition of the resultant alkoxide on the activated azolium, generates a new alcohol (or silyl ether) having incorporated a monomer unit. In the meantime, the NHC catalyst is released and can activate another EO molecule (path A, Scheme 2). The monoadduct, Nu−CH_2CH_2O−E, can serve for subsequent chain propagation. Such a pathway refers to as the activated monomer mechanism.

The fact that $TASF_2SiMe_3$ (**4**) did not yield any polymer in presence of the O-TMS reagent **5** might be in favor of the latter activated monomer mechanism. It was expected indeed that **4** could generate benzylic alkoxide to initiate ROP of EO in case of a chain-end activation mechanism. When used with EO in absence of any other reagent, no polymer was obtained, $TASF_2SiMe_3$ being a too weak nucleophile to directly attack monomer.

Scheme 3. Putative Formation of a Spiro-Type Oxetane Formed by Addition of 1,3-Bis(diisopropyl)imidazol-2-ylidene onto Ethylene Oxide (a) and Reversible Formation of a Spirolactone Reported by Hedrick et al. (b)[83]



The difference between 1,3-bis(diisopropyl)imidazolin-2-ylidene (NHC **3**)—which does not give any PEO despite of being the strongest nucleophile in this series—and the two imidazol-2-ylidenes (NHCs **1** and **2**) allowing organic catalysis of ROP of EO lies in the presence of the unsaturation in the five-member ring of **1** and **2**. In the latter case, and in the event of an activated monomer mechanism, the formation of a zwitterion intermediate must be favored due to the aromatic character of the imidazolium moiety. In contrast, attack of NHC **3** onto EO generates a less stable imidazolinium alkoxide. We postulate that the latter zwitterion can rapidly undergo cyclization, forming a spiro-type oxetane that cannot propagate the polymerization further (Scheme 3). NHC **3** would thus be capable of opening the ring of EO, but this would be followed by the irreversible intramolecular cyclization of the corresponding zwitterion. It has to be mentioned that Hedrick et al. have already reported that spiro-type intermediates can form during ROP of *β*-propiolactone.[83] In this case, however, the cyclic compound is formed reversibly since being of ester type and can be used for chain extension for polyester synthesis. In other words, we tend to give a preference to the activated monomer mechanism on the basis of the results obtained with $TASF_2SiMe_3$ **4** and NHC **3**. However, a thorough investigation would be needed to state on the exact mechanism operating in these NHC-catalyzed ROPs, according to the nature—silylated or hydroxylated—of the chain regulators and the nucleophilicity of the NHC catalyst. Work is in progress to isolate the presumably formed spiro-type oxetane mentioned above.

Conclusion

We propose a novel synthetic route to α,*ω*-difunctionalized PEOs, offering several advantages, among which the use of functionalizing chain regulators such as propargyl or benzyl alcohol or trimethylsilyl nucleophiles, $NuSiMe_3$ (e.g., Nu = N_3 or $PhCH_2O$), an excellent control over molar masses and dispersities, an optimal polymer chain-end fidelity, and the absence of metallic residues through the use of *N*-heterocyclic carbenes (NHCs) as catalysts. This work thus expands the scope of NHCs as viable organic catalysts for polymerization reactions and provides strong arguments that organocatalysis, which is categorized as green chemistry, is a promising way for polymer synthesis. These metal-free NHC-catalyzed ring-opening polymerizations of ethylene oxide were carried out at 50 °C in dimethyl sulfoxide as solvent. Many other OH- or

Me_3Si-containing reagents could be utilized to generate other α,ω-heterodifunctionalized PEOs, which is currently under investigation in our group. Work is also in progress to settle the question of the mechanism of initiation and propagation whether it occurs via monomer activation forming a zwitterionic intermediate or via chain end activation by the NHC through the proton (case of alcohols) or the trimethylsilyl group (case of $NuSiMe_3$) of the chain regulator. This should also depend on the nucleophilicity/silicophilicity/reactivity of the catalyst and the electrophilic character of the monomer and the chain regulator.

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Supporting Information Available: MALDI TOF mass spectrum of α-azido,ω-hydroxy PEO. This material is available free of charge via the Internet at http://pubs.acs.org.

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