DOI: 10.1021/ma901323f

Macromolecules
ARTICLE

Fast Access to Dendrimer-like Poly(ethylene oxide)s through Anionic Ring-Opening Polymerization of Ethylene Oxide and Use of Nonprotected Glycidol as Branching Agent

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Received June 19, 2009; Revised Manuscript Received August 28, 2009

ABSTRACT: Dendrimer-like poly(ethylene oxide)s (PEOs) were synthesized through a semicontinuous process based on the anionic ring-opening polymerization (AROP) of ethylene oxide (EO), followed by AROP of a mixture of glycidol (G) and propylene oxide (PO). Glycidol was used as branching agent generating two hydroxyl groups after ring-opening, whereas propylene oxide served to prevent the aggregation of the generated terminal alkoxides. A three-armed PEO star was first prepared through AROP of EO from 1,1,1-tris(hydroxymethyl)ethane as trifunctional precursor using dimethyl sulfoxide (DMSO) as solvent. After completion of EO polymerization and without isolating the PEO star precursor, G and PO (molar ratio 1:3) were added in the same batch to be polymerized either sequentially or randomly. This led to a three-armed PEO star with an average number of terminal hydroxyls per arm which depended on the number of G units inserted at PEO chain ends, as determined by ^{1}H NMR spectroscopy. Growth of the second and the third generation of PEO could be achieved upon reiterating the same steps of AROP of EO and subsequent AROP of G and PO (arborization step) in one pot, affording dendrimer-like PEOs of generation 3 with moderately distributed but expected molar masses. In a variant of this strategy, G was copolymerized in the presence of allyl glycidyl ether during the arborization step in order to introduce allylic double bonds at the branching points of the dendrimer-like PEOs.

Introduction

Widely acknowledged as the reference biocompatible polymer used in the biomedical field, poly(ethylene oxide) (PEO), also referred to as poly(ethylene glycol) (PEG), possesses unique properties such as chemical stability, solubility in both organic and aqueous media, nontoxicity, low immunogenicity, and antigenicity.[1] PEG has found numerous applications as conjugates to biologically active molecules/substrates (PEGylation), providing the latter with a protection from the immune system and with an enhanced circulation time and efficacy.[1−3] Applications of PEG often use α,ω-heterodifunctional oligomers possessing end functional groups such as amine, carboxylic, thiol, aldehyde, or maleimide to react with a variety of ligands.[1,4−6] However, low molar mass linear PEG precursors with a limited attachment capacity are generally employed. Arranging PEG chains into a branched architecture carrying many reactive sites might offer better performance in biomedical applications than with linear homologues.[2,3,7,8] Branched PEOs possessing a high number of peripheral reacting sites include star-like,[7−15] hyperbranched,[16,17] arborescent,[18−20] or dendrimer-like PEOs.[21−29]

In recent years, we have developed synthetic strategies leading to multihydroxy-ended,[22,23] pH-sensitive,[24] heterodifunctional bouquet-type,[25] and asymmetrical Janus-type dendrimer-like PEOs[26] and to their applications in the biomedical field. Generally speaking, dendrimer-like polymers exhibit structural features similar to those of regular dendrimers, including the presence of a central core, a precise number of branching points, and outer terminal functions, but possess true oligomeric/polymeric segments linking their branching points. The advantages provided by the dendritic structure, in particular its multivalency, can be combined with the unique features of polymers, in the case of PEO its stealth effect.

From a synthetic point of view, dendrimer-like PEOs are synthesized by repeating two elementary steps that are the anionic ring-opening polymerization (AROP) of ethylene oxide (EO) from multifunctional precursors, followed by the arborization (branching reaction) of PEO chain ends.[30,31] However, this branching reaction always requires the specific design of branching agents, making the synthesis of dendrimer-like PEOs tedious as that of regular dendrimers that is achieved stepwise.[21−31]

In this contribution, we explore a shorter divergent synthetic pathway that would allow a fast access to dendrimer-like PEOs by directly using glycidol (G) as a branching agent. Nonprotected G leads to polydisperse hyperbranched polyether polyols, referred to as hyperbranched polyglycerols (HPG), by ring-opening multibranching polymerization (ROMBP). The seminal work by Vandenberg et al.[32] has been further revisited by Mulhaupt, Frey, Haag, and others who developed a slow monomer addition process and the use of partially deprotonated multihydroxy-containing core precursor, in order to achieve better-defined materials in terms of molar masses, degree of branching, and molar masses distribution.[33−40] Here we make use of G for the arborization of PEO chains without resorting to any protection/deprotection steps. A mixture of propylene oxide (PO) and G is indeed directly added at the completion of AROP of EO. The role of PO is to minimize the aggregation of the alkoxides, whereas G generates two hydroxyls through its ring-opening. The number of peripheral hydroxyls and hence the average branching multiplicity are given by the degree of polymerization of the short HPG

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 Published on Web 09/08/2009

Table 1. Molecular Characteristics of Dendrimer-like PEOs of Second Generation and of Corresponding Precursors Obtained Using Glycidol as Branching Agent

sample[a]	conv (%)[c]	$N_{(OH)}$[d]	$M_{n,theo}$[f] ($\times 10^3$)	$M_{n,NMR}$[g] ($\times 10^3$)	PDI
G1a-[HPG$_N$PPO]	60	5.5	5.96	5.20	1.05
G2a		5.5	11.3	11.5	1.06
G1b-[HPG$_N$PPO]	72	12.9	7.83	6.70	1.08
G2b		12.5	13.7	19.9	1.10
G1c-[HPG$_N$PPO]	74	18.2	9.34	7.97	1.10
G2c		18.4	26.2	30.0	1.11
G1d-[HPG$_N$PPO][b]	80	15.3 (2.8)[e]	7.19	5.60	1.12
G2d		14.7 (2.7)[e]	20.6	17.1	1.12

[a] In these notations, the number 1 or 2 represents the generation number, and the letters a to d are meant to distinguish PEO samples of a same series. [b] Glycidol, propylene oxide, and allyl glycidyl ether were introduced as a mixture in the reaction medium; the other samples G1-[HPG$_N$PPO] (a to c) were prepared through sequential addition technique. [c] The conversion of glycidol calculated based on the amount of glycidol added. [d] Number of periphery OH groups generated by arborization of PEO chains and calculated using eq 1. [e] Average number of allyl glycidyl ether units incorporated. [f] M_n calculated based on the amount of the added monomers. [g] Determined using eq 2.

Table 2. Molecular Characteristics of Dendrimer-like PEOs of Second and Third Generation Obtained Using Glycidol as Branching Agent

sample[a]	conv (%)[c]	$N_{(OH)}$[d]	$M_{n,theo}$[f] ($\times 10^3$)	$M_{n,NMR}$[g] ($\times 10^3$)	PDI
G2a-[HPG$_{N'}$PPO]	65	22.0	17.6	14.3	1.24
G3a		24.2	36.3	35.3	1.36
G2b-[HPG$_{N'}$PPO][b]	74	47.3	31.0	26.1	1.38
G3b$_{[N']}$		51.1	73.4	77.4	1.30
G2b-[HPG$_{N''}$PPO]	64	49.5	33.9	24.8	1.27
G3b$_{[N'']}$		57.0	74.3	77.4	1.18
G2c-[HPG$_{N'}$PPO][b]	71	74.0	49.1	45.5	1.18
G3c		78.0	120	131	1.34
G2d-[HPG$_{N'}$PPO]	73	45.6 (7.6)[e]	32.8	20.1	1.28
G3d		47.5 (7.6)[e]	65.7	56.6	1.31

[a] See Table 1 for notation. [b] A mixture of glycidol, propylene oxide, and allyl glycidyl ether was introduced as a mixture in the reaction medium; samples G2-[HPG$_{N'}$PPO] (b and c) were prepared by sequential addition of the monomers. [c] Conversion of glycidol based on the amount of glycidol added. [d] Number of periphery OH groups generated by arborization of PEO chains and calculated using eq 1. [e] Average number of allyl glycidyl ether units incorporated. [f] M_n calculated based on the amount of the added monomers. [g] Determined using eq 2.

sequence formed. We thus propose a one-pot two-step synthetic strategy to dendrimer-like PEOs of second and third generation, combining AROP of EO from partially deprotonated multihydroxylated precursors and use of G as branching agent, in a semicontinuous addition process. In addition, G was copolymerized with allyl glycidyl ether (AGE) so as to introduce allylic double bonds at the branching points of dendrimer-like PEOs.

Experimental Section

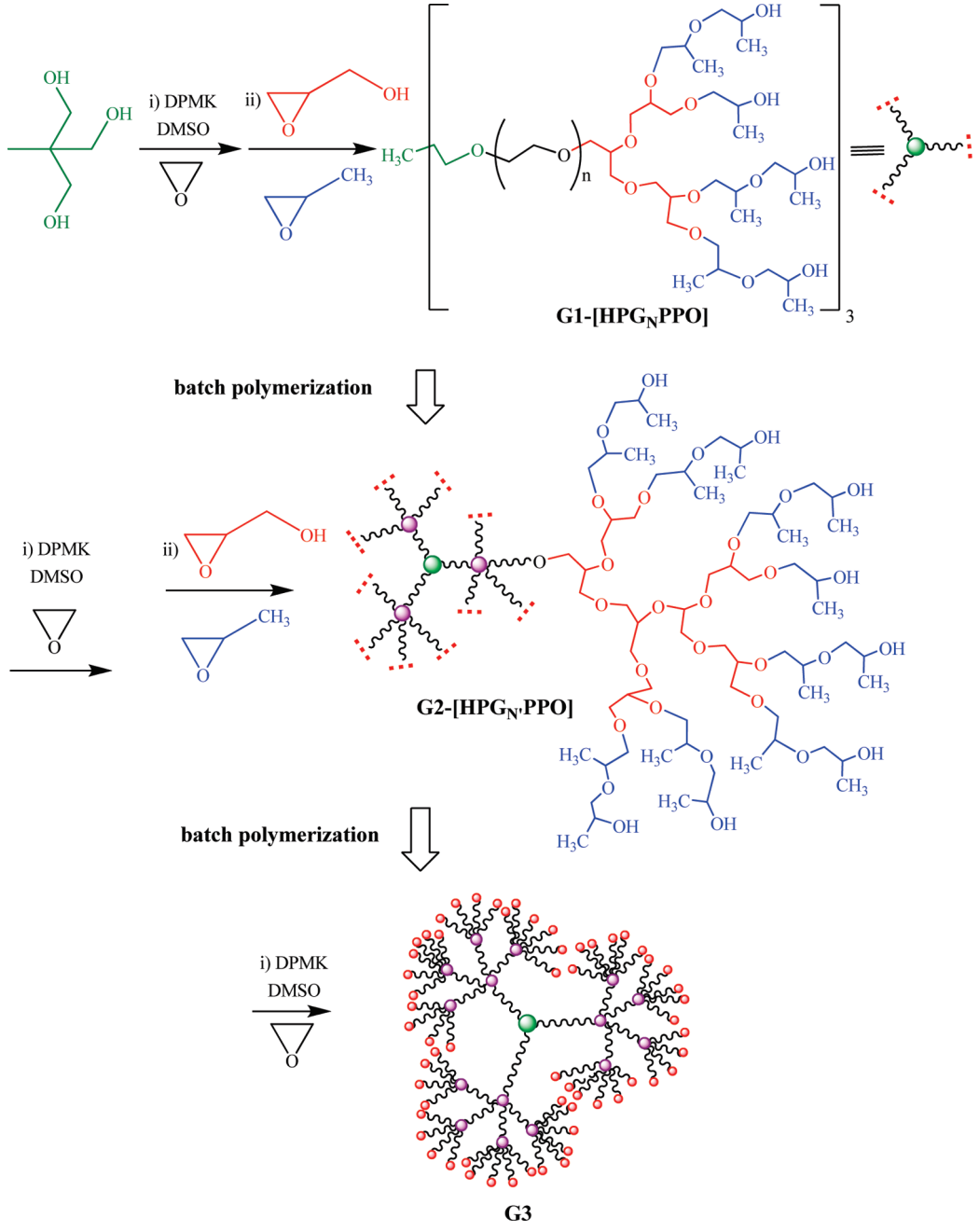
Materials. Ethylene oxide (EO) (Fluka, 99.8%) was distilled over sodium into a buret. Diphenylmethylpotassium (DPMK) was prepared according to known procedures[21,22] and titrated with acetanilide. Glycidol (Aldrich, 99%) was distilled two times under reduced pressure prior to use. Allyl glycidyl ether, propylene oxide, and dimethyl sulfoxide (Aldrich, 99%) were distilled over CaH_2 prior to use. All precursors for the polymerization of EO were dried by freeze-drying from a dioxane solution. In all cases, the PEO derivatives were recovered as white powders. All other chemicals were purchased from Aldrich and used without further purification.

Anionic Ring-Opening Polymerization of Ethylene Oxide Followed by Branching Reaction Using Glycidol and Propylene Oxide. Sequential Polymerization Procedure. Synthesis of G1b-[HPG$_N$PPO] (Table 1). A two-neck 250 mL flask was charged with lyophilized 1,1,1-tris(hydroxymethyl)ethane (80 mg, 6.7×10^{-4} mol) and dry DMSO (20 mL). DPMK (6.0×10^{-4} mol) was introduced so as to deprotonate ~30% of the hydroxyls of the precursor.[21,22] EO (3.4 mL, 68 mmol) was added to this solution, and the polymerization was carried out at room temperature for 3 days. An aliquot was sampled out for analysis. Glycidol (0.74 g, 10 mmol) in a DMSO solution (5 mL) was added with a dosing pump (Becton Dickinson) with a rate of addition of 0.3 mL/h, and the polymerization was carried out at 120 °C under a nitrogen atmosphere. Two hours after adding glycidol, propylene oxide (2.1 mL, 30 mmol) in a DMSO solution (5 mL) was added dropwise with the same rate of addition of 0.3 mL/h. The mixture was cooled to room temperature after addition, and the active species were deactivated by adding a few drops of methanol. The crude solution was first precipitated using an excess of diethyl ether to remove DMSO. The viscous polymer obtained was precipitated twice again in cooled diethyl ether from a THF solution. The polymer (4.2 g, 77%) was collected by filtration and dried at room temperature under vacuum. The data pertaining to the first generation thus synthesized are listed in Table 1.

Random Polymerization Procedure. A typical synthetic procedure of G1d-[HPG$_N$PPO] is as follows. A two-neck 250 mL flask was charged with lyophilized trihydroxymethylethane precursor (64 mg, 5.3×10^{-4} mol) and dry DMSO (20 mL). DPMK (4.8×10^{-4} mol) was introduced so as to deprotonate 30% of the hydroxyls of the precursor. Ethylene oxide (2.7 mL, 54 mmol) was added dropwise onto this solution. The polymerization was carried out at room temperature for 3 days. An aliquot was sampled out for analysis. Glycidol (0.59 g, 8 mmol), allyl glycidyl ether (0.36 g, 3.2 mmol), and propylene oxide (1.1 mL, 16 mmol) in a DMSO solution (10 mL) were added with the Becton Dickinson dosing pump, with a rate of addition of 0.3 mL/h, and the polymerization was carried out at 120 °C under a nitrogen atmosphere. The reaction mixture was allowed to stir for two additional hours after addition of the monomers and the flask was cooled to room temperature. The active species were deactivated by adding a few drops of methanol, and the crude solution was first precipitated in a large excess of diethyl ether to remove DMSO. The viscous polymer obtained was again precipitated twice in cooled diethyl ether from a THF solution. The polymer was collected by filtration and dried at room temperature under vacuum (2.2 g, 52%). The corresponding molecular characteristics are provided in Table 1.

A similar procedure was followed to synthesize the G2a-[HPG$_{N'}$PPO]. Onto a partially deprotonated G1a-[HPG$_N$PPO] precursor (0.98 g, 1.88×10^{-4} mol) in 20 mL of dry DMSO (the extent of deprotonation is equal to 30% using the solution of DPMK), ethylene oxide (1.3 mL, 28.6 mmol) was added, and

Scheme 1. Synthetic Pathway to Dendrimer-like PEOs Using Glycidol and Propylene Oxide during the Arborization Step[a]



[a] Green, violet, and red spots represent the central core, the branching points derived from glycidol, and the OH terminal groups, respectively.

the polymerization was carried out at room temperature for 3 days. A mixture of glycidol (0.40 g, 5.4 mmol) and propylene oxide (1.2 mL, 16.2 mmol) in DMSO (10 mL) was added at a rate of 0.3 mL/h, and the polymerization was carried out at 120 °C under a nitrogen atmosphere. The polymer was recovered using the same procedure as that described above (2.4 g, 68%). The data pertaining to the second generation of dendrimer-like PEOs thus synthesized are provided in Table 2.

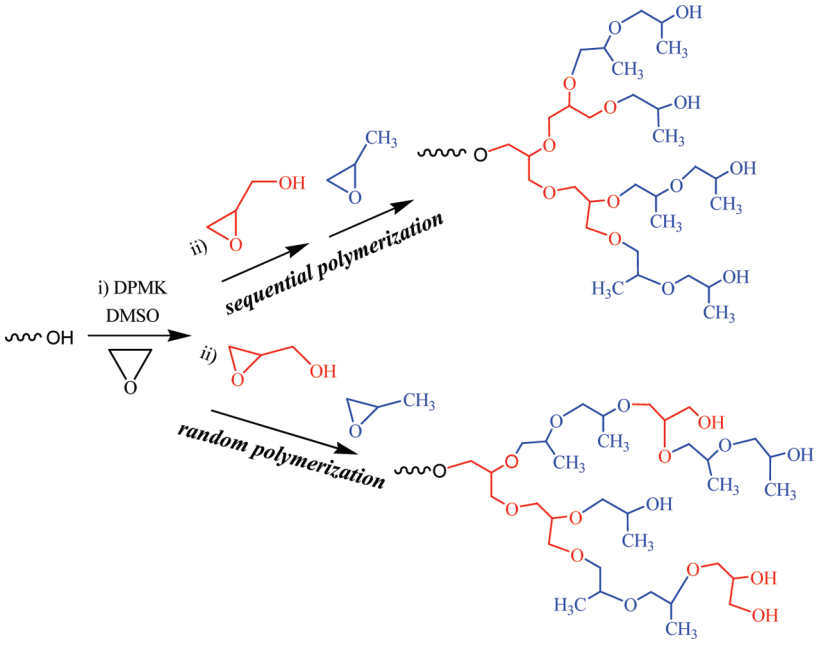
Characterization. ^{1}H NMR spectra were recorded on a Bruker AC 200 spectrometer with $CDCl_3$ as solvent. Size exclusion chromatography (SEC) was performed on a SEC apparatus fitted with one guard column PLGel 5 μm (50 × 7.5 mm) and two PLGel 5 μm MIXED-C columns (300 × 7.5 mm) and a refractive index (RI) detector (Jasco, RI-1530) with DMF (1 g/L LiBr) as eluent (0.8 mL/min) at 60 °C. The apparent molar masses were calculated using linear poly(ethylene oxide) standards.

MALDI-TOF mass spectrometry was performed using a Micromass TofSpec E 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 was first dissolved in THF (10 g L^{-1}). The matrix solution (1,8-dihydroxy-9(10*H*)anthracenone, dithranol) was dissolved in THF. 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.

Results and Discussion

As discussed in our previous studies,[22−26] conditions suitable to polymerize EO from multifunctional hydroxylated precursors

Scheme 2. Effect on the Type of Terminal Hydroxyls after the Arborization Step in the Synthesis of Dendrimer-like PEOs: Statistical vs Sequential Copolymerization of Glycidol and Propylene Oxide



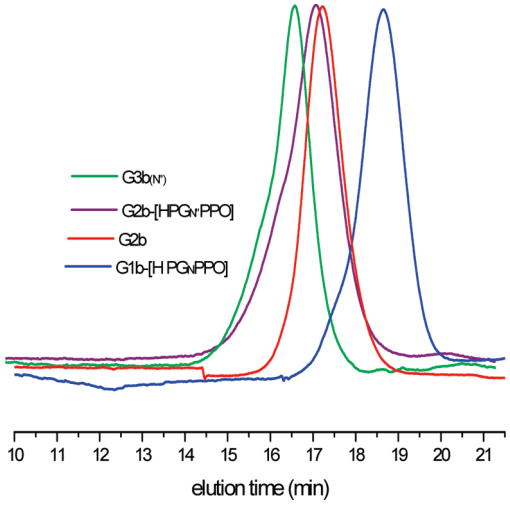


Figure 1. SEC traces of dendrimer-like PEOs from the first to the third generation.

are among others a dissociating medium such as dimethyl sulfoxide (DMSO) and a partial deprotonation of the hydroxyl groups (< 30%) by a solution of diphenylmethylpotassium (DPMK). Because the rate of reversible (degenerative) transfer of protons between active alkoxides and dormant hydroxylated species is much faster than that of propagation,[41,42] this partial deprotonation limits the extent of aggregation. The trifunctional precursor thus used, namely 1,1,1-tris(hydroxymethyl)ethane (**1**), afforded well-defined hydroxy-ended three-armed PEO stars, denoted as G1, following a procedure already reported.[22−26] The key point in our novel synthetic strategy to dendrimer-like PEOs is the introduction of a few glycidol monomer units at the PEO chain ends. Previous reports have described that glycidol (G) can be polymerized under controlled conditions by slowly adding the monomer to a partially deprotonated (10%) multihydroxy-containing core initiator.[33] The concentration of G has to be low enough, however, to avoid the transfer reaction that may occur from active chain ends to the hydroxyl carried by the monomer. For instance, G was directly polymerized from a α-hydroxy-ended linear PEO and PEO-*b*-HPG double hydrophilic block copolymers (DHBCs) were successfully synthesized in this way.[43] In contrast, Dworak et al. in their attempt to polymerize nonprotected G from cesium alkoxides carried by PEO chain end observed chain transfer of propagating alkoxides to the monomer, some HPG homopolymer being formed besides the targeted PEO-*b*-HPG DHBC.[44] The authors therefore resorted to protected G as branching agent to achieve "pom-pom-like" PEOs. In our very first attempts, G was employed alone without propylene oxide (PO) as a comonomer (see further) during the arborization step. The polymerization proceeded as expected, affording a compound denoted G1-[HPG$_N$], where N is the average number of terminal hydroxyl groups. This compound served as precursor of the second generation of PEO, G2, which could be readily achieved after AROP of EO. The SEC trace of G2 indeed exhibited a unimodal and symmetrical distribution. However, when repeating the same sequence of reactions, that is, the AROP of G and of EO in this order, the dendrimer-like PEOs of second and third generation exhibited SEC traces of broader molar mass distribution and a shoulder peak in the low molar mass region. Very likely, not all terminal hydroxyls or alkoxides of the corresponding precursors were accessible and available for EO initiation. This was also observed by Frey and Lutz et al. in their attempt to derive multiarm PEO stars from HPGs used as multifunctional macroinitiators.[14] To prevent that self-aggregation of the growing alkoxides affects the initiation step, these authors proposed to introduce several hydrophobic PO units before growing PEO arms.[14] We thus adapted this procedure for the arborization of PEO chain ends, through either the sequential or the statistical copolymerization of G and PO at 120 °C, using DMSO as solvent (Scheme 1). The presence of a few PO units at PEO chain ends combined with a partial deprotonation of hydroxyls (30%) indeed minimized the self-aggregation of alkoxides, which proved helpful to grow the next generation of PEO under controlled/living conditions. As one G generates two hydroxyls after ring-opening, two G monomer units generate three hydroxyls in total and so on: the average number of terminal hydroxyls per PEO arm ($N_{(OH)per\ arm}$) of the targeted structure, denoted G1-[HPG$_N$PPO], thus corresponded to the

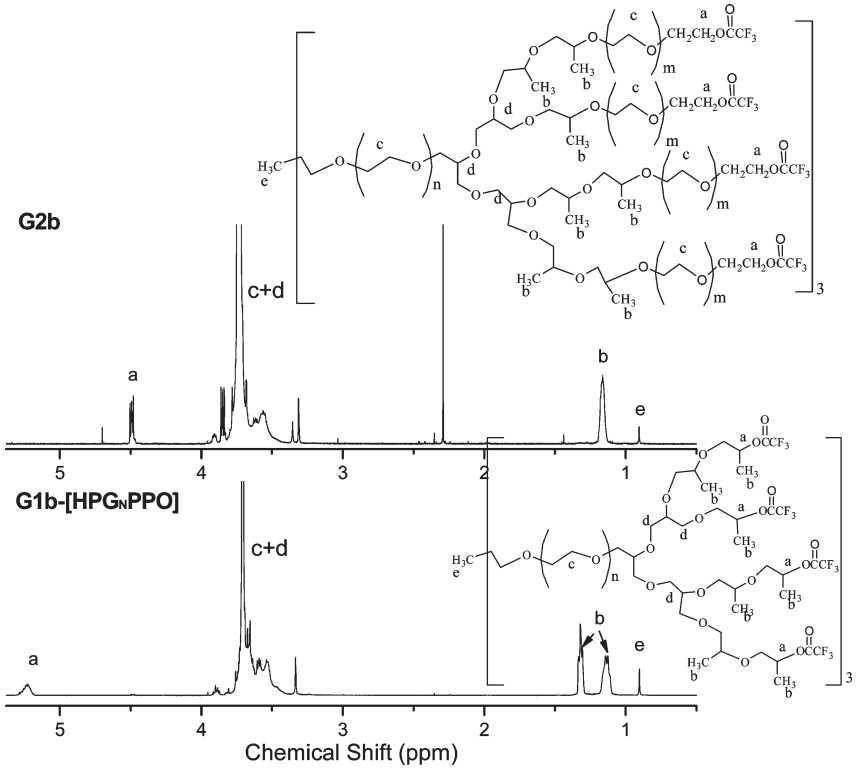


Figure 2. ^{1}H NMR spectrum ($CDCl_3$ + trifluoroacetic anhydride) of the second generation G2b dendrimer-like PEO and its precursor G1b-[HPG$_N$PPO], allowing for the determination of the content in terminal hydroxyls (Table 1).

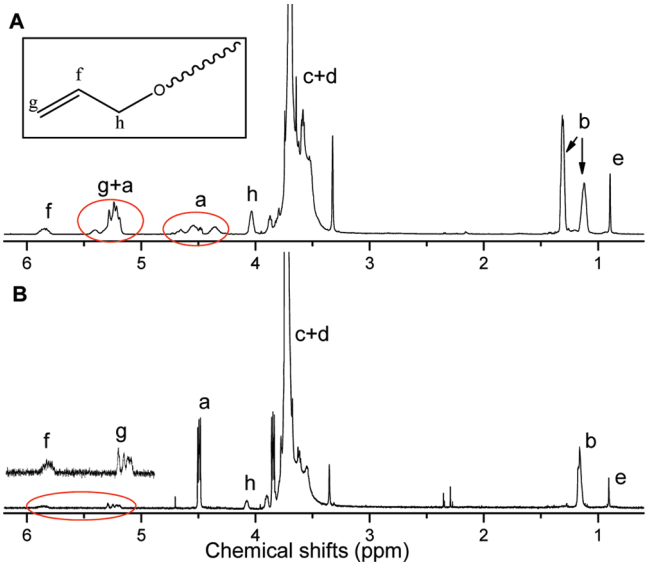


Figure 3. ^{1}H NMR characterization of the second generation G2d dendrimer-like PEO (B) and its precursor G1d-[HPG$_N$PPO] (A) synthesized using glycidol, propylene oxide, and allyl glycidyl ether during the arborization step.

total amount of G polymerized (N_G) plus one: $N_{(OH)\text{per arm}} = N_G + 1$ (see Scheme 2). The same two-step sequence of polymerization of EO followed by arborization of PEO chain ends through copolymerization of G with PO was repeated to grow the second PEO generation, affording a dendrimer-like sample, noted G2-HPG$_{N'}$PPO. In the same way, a third generation of PEO was grown, affording G3 with an average number molar mass up to 55 000 g/mol and a polydispersity of 1.31 (Scheme 1 and Table 2).

As shown in Figure 1, narrow SEC traces were obtained from the first to the third generation. In Tables 1 and 2 are summarized molecular features of all PEO dendrimer-like samples prepared and their precursors. No major difference is observed between the dendritic PEO samples for which branching points were generated from the sequential or the random copolymerization of G and PO. The only difference is actually the type of hydroxyls present at PEO chain ends of the precursor, as shown in Scheme 2: only secondary hydroxyls are formed when G and PO are sequentially copolymerized during the arborization step, whereas both primary and secondary hydroxyls result from the random copolymerization of the two monomers.

Molar masses as well as the average number of peripheral hydroxyl groups of the PEO derivatives could be determined by ^{1}H NMR spectroscopy. In particular, the content in hydroxyl groups was evaluated after their derivatization into trifluoroesters using trifluoroacetic anhydride. In Figure 2, for instance, the ^{1}H NMR spectrum of G1-[HPG$_N$PPO] precursor of the dendrimer-like PEO of second generation, G2b, shows the signals of both the methylene ($-CH_2O-$) and the methine ($-CH(CH_2O-)OH-$) protons due to the resonance of the primary and the secondary derivatized trifluoroesters at 4.48 and 5.22 ppm, respectively, without interference with other signals.

The methyl protons of the core still can be detected at 0.90 ppm. Signals due to the protons of PO units appear at 1.32 and 1.13 ppm for methyl protons, whereas methylene and methine protons overlap with the PEO signal from 3.7 to 3.4 ppm. One can also note that the two signals of the methyl protons of PO units merged as one peak at 1.17 ppm for G2b. This is likely due to the change in the chemical environment of the methyl protons before and after the growth of PEO arms of the second generation: the precursor indeed carried trifluoacetic ester groups attached to the asymmetric carbon of the terminal PO unit, whereas in the second generation dendrimer-like PEO the same ester linkages are separated with ether ones. The ratio of integration of the peaks at 4.48 and 5.22 ppm mentioned above to that of the peak due to the methyl protons of the core at

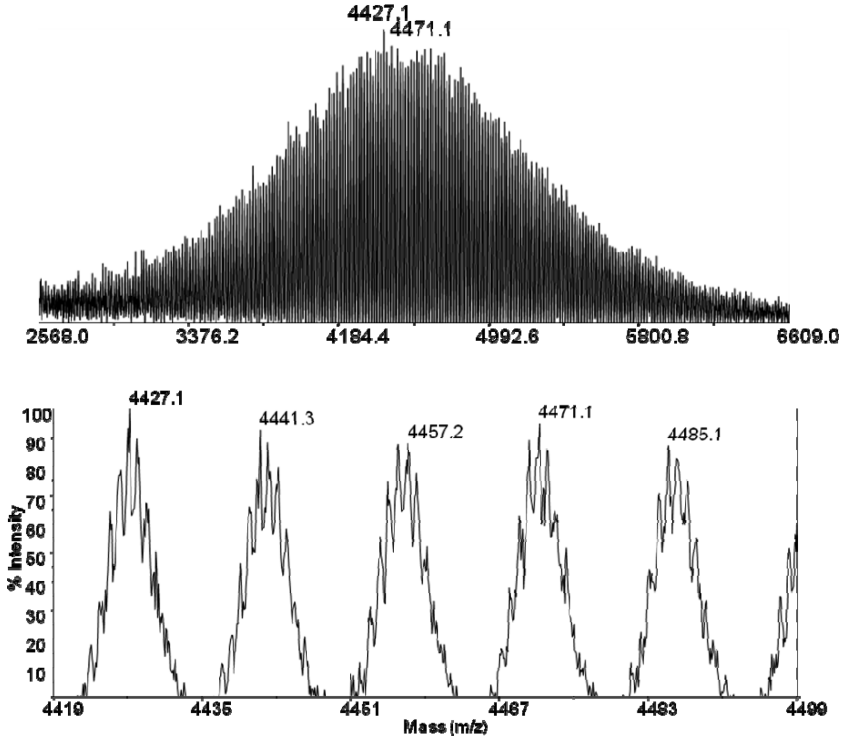


Figure 4. MALDI TOF mass spectrum of G1a-[HPG$_N$PPO].

0.90 ppm helped us to deduce the number and the type of hydroxyl groups (*N* number in Table 1).

When randomly copolymerized during the arborization step, G and PO are expected to generated two types of randomly distributed terminal hydroxyls (Scheme 2). As anticipated, two broad peaks attributed to the corresponding trifluoroesters appeared around 4.60 and 5.30 ppm (Figure 2). Upon initiation of EO from the two types of deprotonated hydroxyls, however, only primary alkoxides are generated. The total number of hydroxyls thus calculated after both arborization and growth of the second generation of PEO chains remains constant, indicating that initiation took place from all of the hydroxyls (Tables 1 and 2). In this way, the number of terminal OH and hence the number of arms of each generation of PEO could be adjusted upon varying the amount of G added.

From ^{1}H NMR characterization and precisely, from the peak due to trifluoroesters, the number of peripheral hydroxyl groups is calculated using the following equation:

$$N_{(OH)} = (3I_{5.3}/I_{0.9})+(3I_{4.5}/2I_{0.9}) \quad (1)$$

where $I_{5.3}$ and $I_{4.5}$ represent the signal intensity of terminal methylene and methine protons connected to trifluoro groups, respectively, and $I_{0.9}$ is the intensity of the core methyl signal at 0.90 ppm. The total molar mass of the PEO is thus equal to the sum of the molar mass of the three constitutive units, PO, G, and EO, according to eq 2:

$$M_{n(NMR)} = M_{n(PPO)}+M_{n(PGly)}+M_{n(PEO)} \quad (2)$$

with

$$M_{n(PPO)} = 56(I_{1.3-1.1}/I_{0.9})$$

$$M_{n(PGly)} = 74(N_{(OH)}-3)$$

$$M_{n(PEO)} = 120+44 \times 3[I_{3.6}-I_{1.3-1.1}-5(N_{(OH)}-3)I_{0.9}/3]/4I_{0.9}$$

$I_{1.3-1.1}$, $I_{0.9}$, and $I_{3.6}$ being the integral of the peaks due to PO units, the initiating core, and EO units, respectively; the values 120, 56, 44, and 74 are the molar mass of 1,1,1-trihydroxymethylethane, PO, EO, and glycidol, respectively (Tables 1 and 2).

Finally, functional groups could be introduced at the interior of dendrimer-like PEOs using a functional comonomer, namely, allyl glycidyl ether (AGE), during the arborization step. The incorporation of functional groups at the interior of regular dendrimers has already been exploited to finely tune their physical properties and target specific applications or to favor intramolecular reaction by a concentration effect.[45] In addition, we have recently reported the first example of poly(acrylic acid)-containing dendrimer-like PEOs that were obtained through the functionalization of their interior with allylic groups using an AB_2C-type branching agent.[24] In the present work, the three monomers (G, PO, and AGE) were slowly added onto the living alkoxides of the PEO arm ends, in order to generate both allyl-containing branching junctions and the hydroxyl groups required to grow the next generation. Average numbers of three and five allyl groups were respectively introduced (Tables 1 and 2). A typical ^{1}H NMR spectrum of a functionalized dendrimer-like PEO is shown in Figure 3.

The peaks characteristic of the allylic protons (f, g, h) can be seen at 5.85, 5.25, and 4.08 ppm, respectively. These double bonds can be readily derivatized into other functional groups as reported previously.[24]

Characterization by MALDI TOF mass spectroscopy of these branched PEOs is a challenging task owing to the presence of three types of monomer units (EO, G, and PO) whose number can fluctuate from one branched macromolecule to another. In addition, it is important to note that in the present case the molar mass of three EO units coincidently equals the molar mass of one G unit plus that of one PO unit: 3 × EO = G + PO = 132 g mol^{-1}. This obviously complicates further the MALDI TOF mass spectra of these PEO derivatives, and therefore the data interpretation should be made with caution. A representative MALDI TOF spectrum of the G1a-[HPG$_N$PPO] sample is shown in Figure 4. First, the parent three-arm PEO star that served as precursor to G1a-[HPG$_N$PPO] before addition of G and PO should give, if present, a main peak in the enlarged region

appearing at $m/z = 4460.60$. This population being not observed, one can assume that all of the three hydroxyls of this parent PEO have been utilized during the arborization step, as also supported by the ^{1}H NMR monitoring discussed above. Next, the different series of peaks shown in the enlarge region of Figure 4 can be explained as follows. For example, the peak at $m/z = 4457.16$ g mol^{-1} is likely the result of the following structure: $EO_{88}G_2PO_5$ whose molar mass equals $88 \times 44.05 + 2 \times 74.08 + 5 \times 58.08 + 120 + 23$, where 120 and 23 are the molar mass of the trifunctional core precursor and of sodium ion, respectively, 44.05, 74.08, and 58.08 being the molar mass of EO, G, and PO, respectively. Similarly, the peaks at $m/z = 4471.13$ and $m/z = 4485.14$ could be attributed to the structures $EO_{87}G_2PO_6$ and $EO_{87}G_3PO_5$, respectively.

In reality, a particular ion peak could be ascribed to different combinations of the three monomer units. For example, the peak mentioned above at $m/z = 4457.16$ g mol^{-1} can also result from the following combinations: $EO_{91}G_1PO_4$ or $EO_{85}G_3PO_6$ or $EO_{82}G_4PO_7$ or $EO_{79}G_5PO_7$, etc. However, if one considers that this peak does derive from a parent three-arm star with 88 EO units and since the NMR results gave an average number of 5.5 terminal OH corresponding to 2.5 units of G polymerized, one can reasonably conclude that the most probable combinations for this ion peak are $EO_{88}G_2PO_5$, $EO_{88}G_2PO_6$, and $EO_{88}G_3PO_5$.

Conclusion

We propose a fast and versatile two-step synthetic strategy to dendrimer-like poly(ethylene oxide)s (PEOs) with high loading capacity that relies on an iterative divergent method, combining two elementary steps that are (i) the anionic ring-opening polymerization of ethylene oxide (AROP of EO) and (ii) the semicontinuous and slow addition of a commercially available branching agent, namely nonprotected glycidol, during the arborization step of PEO chain ends. Random or sequential copolymerization of propylene oxide with glycidol, in addition to a low degree of deprotonation of hydroxyl groups, and use of DMSO as a solvent are the appropriate conditions to avoid the formation of aggregates during the AROP of EO from multihydroxylated precursors. A series of dendrimer-like PEOs up to generation 3 with an average number molar mass up of 55 000 g/mol and a polydispersity of 1.31 could thus be synthesized. This strategy does not require any protection/deprotection step, and only an intermediate purification by precipitation is necessary before growing the next generation of PEO. Alternatively, allyl glycidyl ether can be readily copolymerized with propylene oxide and glycidol in order to introduce allylic groups during the arborization step; this offers possibilities for further functionalization/derivatization of the interior of these dendrimer-like PEOs. Thus, advantages provided by the dendritic scaffold, in particular its multivalency due to the presence of numerous hydroxyl terminal groups, can be easily combined with the very unique features of PEO.

Acknowledgment. The authors are grateful to the Centre National de Recherches Scientifique (CNRS), the French Ministry of High Education, and a NIH grant (program 5R01 RR14190-04) that helped support X.F.

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