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Radical Chain End Chemical Transformation of SG1-Based Polystyrenes

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ABSTRACT: Radical chain end functionalization of polystyrene previously prepared by NMP using the SG1 nitroxide was investigated. Hydroxy-functional polystyrenes were easily prepared by two different pathways: via an exchange with TEMPO nitroxide followed by a Zn/AcOH reduction or via a radical hydroxylation using the *in situ* preparation/reduction of the corresponding hydroperoxide. The introduction of a bromine end group was performed by radical bromination under mild conditions using ethyl 2-bromoisobutyrate as bromine transfer agent. The latter polymer was further reacted with NaN_3 and also used as a macroinitiator to prepare PS-*b*-PMMA by ATRP to confirm the chemical post-transformation. Azide-functional polystyrenes were also prepared by a one-step radical azidation reaction using ethanesulfonyl azide. In all cases, the chemical transformations were followed by both liquid chromatography at the critical condition in pure eluent and Maldi-Tof MS.

Introduction

With the development of the living/controlled radical polymerization (CRP) techniques,[1] such as nitroxide-mediated polymerization[2−5] (NMP), atom transfer radical polymerization[6−9] (ATRP), and reversible addition−fragmentation chain transfer[10−13] (RAFT), the control of the structure and architecture of vinyl polymers exhibiting specific properties is now possible in many cases.

Despite the significant progress made in the elaboration of complex macromolecular architectures using CRP methods, the preparation of well-defined polymer chains containing groups with different polarity and reactivity from backbone is still highly desired. Indeed, these functionalized polymer chains are very useful as building blocks in many applications.[14−20] Therefore, the synthesis of functional polymers became recently an important aspect of CRP studies. The easiness of preparing α,ω-functionalized polymers or "telechelic" polymers varies importantly depending on the controlled technique used.[21] α-Functionalization of the polymer chains is readily obtained by preparing the corresponding initiator prior to polymerization.[22,23] In that case ATRP is probably the more convenient technique since a large range of α-brominated ester or amide compounds is either commercially available or easy to prepare. Functionalized alkoxyamines could be prepared but need generally multisteps syntheses. Regarding the α-functionalization, the RAFT process is very likely the less convenient technique since to reach 100% of α-functionality, both the transfer agent and the radical initiator have to be functionalized prior to the polymerization step due to its inherent mechanism.

The ω-functionalization is mostly more difficult to perform since it requires chemical transformation after the polymerization step. For that purpose, ATRP is the more straightforward CRP technique. Indeed, the nucleophilic substitution[22] of the halogen end group could be carried out with numerous reactants such as sodium azide, ethanolamine, sodium acrylate, etc. Recently, Sawamoto et al.[24] introduced a new "umpolung" procedure to favor the nucleophilic substitution when the latter was difficult to perform. The thiocarbonylthio function of a RAFT polymer could be transformed by different ways into a thiol group.[25−32] This reactive group is widely used to prepare bioconjugates[33] and to conduct the thiol−ene coupling "click" reactions.[34−36] The introduction of other functional group is possible but is restricted to the ones availables in azo compounds.[37]

Unlike ATRP and RAFT, the removal or transformation of the nitroxide moiety in NMP has not been extensively studied.[38−41] The first example was presented by Rizzardo,[4] who reduced the TEMPO to an hydroxy end group using a mixture of Zn/acetic acid. Pionteck et al.[42] extended this result on the TEMPO moiety with different oxidative and reductive agents. Hawker et al.[43] used a radical approach based on a non-self-polymerizable monomer (maleimide, maleic anhydride). In this system, only one unit could be added, and this step is followed in situ by an elimination of the TIPNO nitroxide. A similar approach was developed by Braslau using TIPNO-based polymers and benzyl enol ether as radical trap.[38]

Despite the importance of the acyclic β-phosphorylated nitroxide SG1 (*N*-*tert*-butyl-*N*-[1-(diethoxyphosphoryl)-2,2-dimethylpropyl-*N*-oxyl nitroxide) and its corresponding alkoxyamine Blocbuilder in the field of NMP[44] (control of styrenes, acrylates, acrylamides, and methacrylates derivatives (using the copolymerization approach[45]); commercial availability of the alkoxyamine Blocbuilder), surprisingly no work has been published on the ω chain end transformation of polymers prepared using this technology. This prompted us to develop methodologies to achieve ω-functionalized polymers as precursors to complex architectures, in the case of polymers previously prepared using SG1 and the corresponding alkoxyamine BlocBuilder.[46−48]

However, we showed in this paper that the methods already developed for TEMPO or TIPNO nitroxide could not be extrapolated to SG1, and new reactions have to be designed. The introduction of functionality in the ω-position was then investigated via the radical reactivity of the SG1 macroalkoxyamine. Our strategy was to extrapolate different radical reactions already developed for radical organic chemistry to SG1 end-capped polystyrenes (PS-SG1) (Scheme 1).

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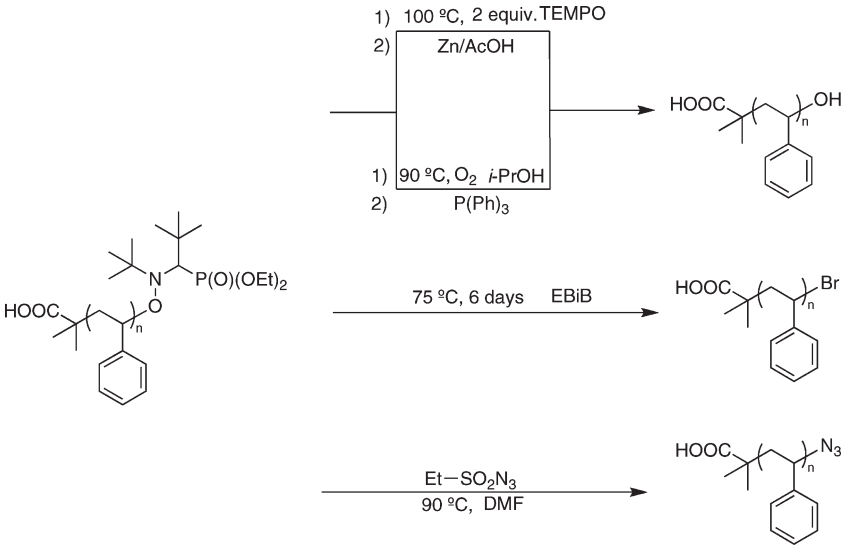
Scheme 1. End-Functional Polystyrene Prepared from a PS-SG1 Precursor



Terminal hydroxy-functional polystyrene was prepared using two procedures: (1) a selective nitroxide exchange with TEMPO followed by a reduction reaction and (2) a "one-pot" radical hydroxylation reaction. Second, the introduction of a halogen end group and specially a bromine atom was performed in mild condition using ethyl 2-bromoisobutyrate (EBiB). The PS-Br was then reacted to confirm the functionalization: the nucleophilic substitution using NaN_3 to prepare the azide-terminated polymer and the ATRP polymerization to prepare the PS-*b*-PMMA block copolymer. Finally, the preparation of azide-functional polystyrene was conducted by "one-pot" radical azidation using ethanesulfonyl azide. In all case the reactions were monitored by Maldi-Tof to identify the end group and by liquid chromatography at the critical condition in pure eluent LC-CC to quantify the yield of the reaction.

Experimental Section

Materials. All reagents were used without further purification. Polystyrene PS-SG1 (4900 g mol^{-1}, PDI = 1.22) was prepared as previously described.[46] Sodium azide NaN_3 (> 99.5%), TEMPO (98%), ethyl 2-bromoisobutyrate EBiB (98%), *N*-bromosuccinimide (99%), triphenylphosphine $P(Ph)_3$, zinc powder, and acetic acid were purchased from the Aldrich Chemical Co. Ethanesulfonyl azide was prepared according to the procedure of Renaud.[49]

Instrumentation. The SEC experiments were performed on a setup previously described.[46] The LC-CC experiments were performed on a Varian PL-GPC 120 apparatus, which was composed of an Agilent 1100 series pump, a degasser, and a RI detector. The following columns were used: Macherey & Nagel 250 mm × 4.6 mm Nucleodur C18 Gravity, pore diameter 110 Å, particle size 3 μm and Macherey & Nagel 250 mm × 4.6 mm Nucleodur C18 Gravity, pore diameter 110 Å, particle size 5 μm. The injection loop, the columns, and the RI detector were in the same thermostated oven. The eluent was dimethylformamide, filtered on a 0.2 μm Nylon Alltech membrane. The samples were dissolved in DMF at 0.25 wt % before being filtered on a 0.2 μm Nylon Alltech filter. The flow rate was fixed at 0.8 mL min^{-1}.

MALDI-TOF MS experiments were carried out using a Bruker Autoflex (Bruker Daltonics, Leipzig, Germany). The instrument is equipped with a nitrogen laser emitting at 337 nm, a single-stage pulsed ion extraction source, and dual microchannel plate detectors for linear and reflectron modes. Positive-ion mode was used for all analyses with an accelerating voltage of 19 kV for reflectron mode. The MALDI mass spectra represent averages over 300 consecutive laser shots (10 Hz repetition rate). Two procedures were used for the sample preparation. A solid deposition was used for macroalkoxyamine PS-SG1 and PS-TEMPO whereas a liquid deposition was used for the functionalized polystyrene. The solid deposition consists in the milling of the sample (1−2 mg) with 2,5-dihydroxybenzoic acid DHB (8−9 mg) followed by a deposition of the powder onto the sample target. In the case of liquid deposition, the polystyrene solutions (11.6 g L^{-1}) were prepared in THF. The matrix *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) was also dissolved in THF (10 g L^{-1}). The polystyrene solution (2 μL) was mixed with 70 μL of the matrix solution. 1 μL of a silver trifluoroacetate solution (10.4 g L^{-1} in THF) was then added to favor ionization by cation attachment. A 1 μL portion of the final solution was deposited onto the sample target and allowed to dry in air at room temperature. Internal standard (PMMA 4030 Da) was used to calibrate the mass scale.

Nitroxide Exchange. PS-SG1 (2.5 g, 0.51 mmol) and TEMPO (156 mg, 1.02 mmol) in 20 mL of *tert*-butylbenzene were introduced in a 100 mL round-bottom flask. The flask was purged with dry N_2 gas and heated at 100 °C for 2 h. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

PS-TEMPO Reduction. PS-TEMPO (530 mg, 0.1 mmol) and Zn powder (200 mg, 3 mmol) in 50 mL of THF/acetic acid (70:30 v:v) were introduced in a 100 mL round-bottom flask. The flask was heated at reflux for 3 h. Four additions of 100 mg of Zn were introduced during the reaction. After dilution with 30 mL of THF, the Zn powder was removed by Celite filtration. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

Radical Hydroxylation. PS-SG1 (1.25 g, 0.25 mmol) in 20 mL of *tert*-butylbenzene was introduced in a 100 mL round-bottom flask. The flask was bubbled with air and heated at 90 °C overnight. 112.5 mg of triphenylphosphine was then added, and the medium was stirred overnight at room temperature. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

Radical Bromination. PS-SG1 (200 mg, 4.1×10^{-5} mol) and 3 mL of ethyl 2-bromoisobutyrate were introduced in a 50 mL round-bottom flask. The flask was purged with dry N_2 gas and heated at 75 °C for 6 days. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

Nucleophilic Substitution. A solution containing PS-Br prepared by radical bromination (200 mg, 4.1×10^{-5} mol) and sodium azide (13 mg, 0.2 mmol) in 4 mL of dimethylformamide were mixed in a 30 mL round-bottom flask at room temperature

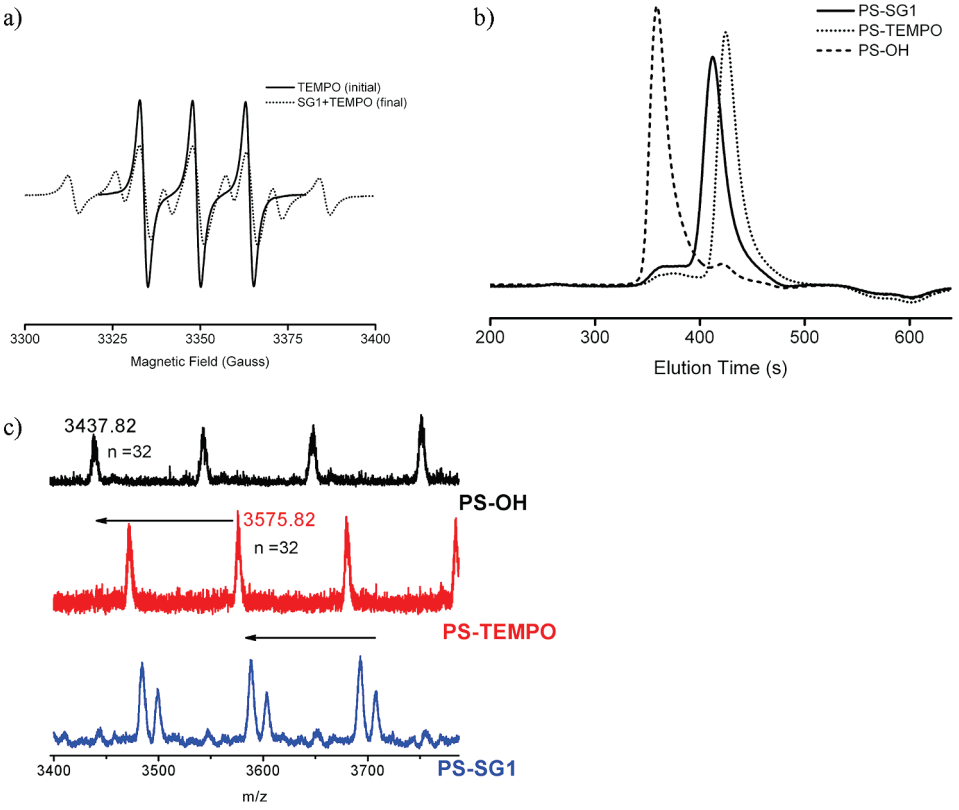


Figure 1. (a) ESR spectrum obtained during the nitroxide exchange reaction (100 °C, 2 equiv of TEMPO, 2 h). (b) LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the exchange/reduction reaction. (c) Maldi-Tof analysis of the exchange/reduction reaction.

for 2 h. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

Preparation of PS-*b*-PMMA by ATRP. CuCl (2.5 mg) and dNbpy (20 mg) were placed in a round-bottom flask, which was then purged with argon. Methyl methacrylate (1 mL, 9.36 mmol) and diphenyl ether (0.9 mL) were introduced into the flask via an Ar-washed syringe. The flask was then placed in an oil bath at 90 °C and the solution stirred until homogeneous. PS-Br (230 mg, 4.7×10^{-5} mol) was first dissolved in a small amount of solvent (0.1 mL) and then added to the flask via a syringe. The polymer was purified by dissolving in THF and passing through an alumina column and then isolated by precipitation into methanol and dried under vacuum.

Radical Azidation. PS-SG1 (100 mg, 2.05×10^{-5} mol) and 970 mg of ethanesulfonyl azide (7.17 mmol) in 3 mL of *N,N*-dimethylformamide was introduced in a 100 mL round-bottom flask. The flask was purged with dry N_2 gas and heated at 90 °C for 3 days. The polymer was then purified by precipitation in cold methanol and dried over vacuum.

Results and Discussion

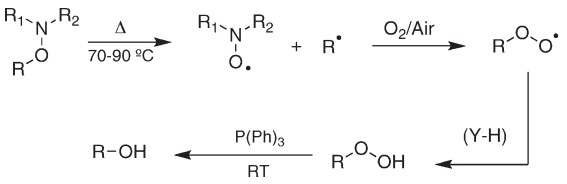
Alkoxyamines or macroalkoxyamines bearing the TEMPO moiety could be easily reduced by either a mixture of Zn/AcOH or $LiAlH_4$ leading to a terminal hydroxy-functionalized polystyrene.[4,42] Pionteck et al.[42] showed as well that the end-capped TEMPO polymers could be oxidized at room temperature by *m*-chloroperbenzoic acid (*m*CPBA) to produce a ketone-terminated polymer. Extrapolation of either the oxidation or reduction methods to polystyrenes bearing a SG1 as end group was nonconclusive. Indeed, in each case the experiments only lead to the starting polymers as checked by ^{31}P NMR and liquid chromatography at the critical condition LC-CC.

Braslau et al.[39] developed a single electron oxidation of the *N*-alkoxyamine based on the TIPNO nitroxide using ceric ammonium nitrate (CAN) to form secondary benzylic cations at the polymer terminus. The same procedure was used with PS-SG1 and led again to the starting polymer. In a similar manner, samarium iodide SmI_2 reduction was also inconclusive. From these results, one can assume that reactivity of SG1 (macro)alkoxyamine toward reducing or oxidating agents is different from TEMPO- or TIPNO-based (macro)alkoxyamines. This behavior, probably related to the combination of the polar effect due to the phosphorylated group and the steric effect, is currently under investigation in our group. To overcome this problem, we decided to take advantage of the radical reactivity of the macroalkoxyamine to introduce functional groups.

Synthesis of Hydroxy-Terminated Polystyrene. We investigated different radical pathways allowing the replacement of the SG1 moiety by an alcohol function. The first method is based on a two-step process. The first step would consist of exchanging the SG1 nitroxide with the TEMPO followed by the already reported reduction reaction for TEMPO−polystyrene chains (Scheme 1). We investigated also a more straightforward procedure based on a radical hydroxylation reaction.

Turro,[50] Scaiano,[51] and Hawker[52,53] studied the nitroxide exchange between polystyrene end-capped with the TEMPO moiety and 4-substituted TEMPO derivatives. In all cases, the exchange is performed between functionalized and non-functionalized nitroxides but having the same radical reactivity, implying the use of a large excess of free nitroxide. Our strategy is based on a nitroxide exchange where the final macroalkoxyamine based on TEMPO is more stable than the starting one based on the SG1 moiety. The exchange was thus performed at 100 °C with only 2 equiv of TEMPO. The reaction was monitored by electron spin resonance (ESR). After 2 h of reaction, the observed ESR spectrum was a combination of the ESR spectrum characteristic of SG1 and the one of TEMPO in a ratio 1:1 (Figure 1a), indicating a near-quantitative yield for the exchange reaction.

Scheme 2. Radical Hydroxylation Reaction



After purification by precipitation in cold methanol, the prepared polymer was reduced using a mixture of Zn/AcOH as described by Rizzardo et al.[4] LC-CC in pure eluent was used to monitor the reduction reaction. Previously, we showed that polystyrene could be eluted at the critical conditions in pure dimethylformamide (DMF) at temperatures above 70 °C, and therefore functional polystyrenes could be separated.[54] In our case, the optimal temperature was found equal to 82.5 °C. The chromatograms obtained after injection of PS-SG1, PS-TEMPO, and PS-OH are presented in Figure 1b. As already observed,[54] the PS-SG1 chromatogram presents a small ill-defined shoulder at lower retention time (370 s), which has been attributed to recombination products bearing two polar carboxylic acid moieties. These dead chains represented 5−15% of the whole chromatogram. As the column used for the analysis is apolar (C_{18}) and the TEMPO moiety is less polar than the SG1 moiety, it can be seen that the chromatogram is quantitatively shifted toward higher elution volume after the first step and shifted toward lower elution volume when the polar hydroxy group is introduced.

The end-group identification was further confirmed by mass spectrometry. MS analyses have already proven to be a valuable tool to investigate the mechanism of controlled radical polymerization.[55−57] The two most common mass spectrometry techniques for the analysis of polymers are matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI TOF) and electrospray ionization mass spectrometry (ESI-MS). For the analysis of polymers made by NMP, ESI-MS was shown to be more efficient since degradation of the nitroxide moiety could occur during the gas phase ionization process.[58,59] In our case, the ESI-MS technique could not be used because of the mass range accessible by this technique is limited below 2000−3000 Da.[55] The spectra for the polystyrenes before and after the two-step procedures are presented in Figure 1c.

The mass spectrum of the PS-SG1 sample presented two distributions, with a 60/40 ratio. The first one exhibited a molar end group of $(47.5 + n \times 104.1)$ g mol^{-1} and a second one of $(62.3 + n \times 104.1)$ g mol^{-1}. None of them could be clearly related with the expected structure bearing one SG1 end group (i.e., 381 g mol^{-1}). Ladavière et al.[60] recently investigated the analysis of polystyrene prepared by different CRP techniques and especially by SG1-mediated polymerization. They concluded that the observation by Maldi-Tof MS of PS-SG1 could not be achieved whatever the analytical condition. After the nitroxide exchange, the mass spectrum exhibited only one distribution in agreement with a quantitative exchange reaction. The molar mass of the end group is equal to 243.5 g mol^{-1} for a theoretical value of 243.2 g mol^{-1} ($(CH_3)_2C(COOH)$ 87.0 g mol^{-1} + TEMPO 156.2 g mol^{-1}), confirming both the quantitative exchange and the fragmentation of the SG1 moiety during the Maldi-ToF analysis. The polymer after reduction was also analyzed. The Maldi spectrum presented one distribution with a molar mass end group of 103.5 g mol^{-1} for a theoretical value of 104.0 g mol^{-1}. The result shown in Figure 3 confirmed the one obtained by LC-CC, that is, a quantitative hydroxy functionalization of the starting PS-SG1. This result showed that the preparation of polystyrene end-functionalized by an hydroxy group can be performed quantitatively using a two-step procedure.

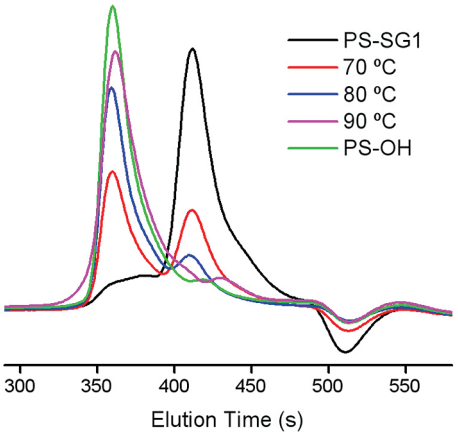


Figure 2. Influence of the reaction temperature on the yield of PS-OH during the radical hydroxylation reaction (LC-CC, DMF, 82.5 °C, C18 nucleodur columns).

In order to develop a more straightforward method than the one presented previously, we investigated the method developed by Barton et al.[61,62] to introduce an OH group on an alkyl radical moiety. This approach is first based on the trapping of the alkyl radical by dioxygen and the subsequent formation of hydroperoxide after reaction with a hydrogen donor. The latter compound is reduced by triphenylphosphine ($P(Ph)_3$) at room temperature in a one-pot procedure (Scheme 2).

Inspired by this work, we heated overnight the PS-SG1 macroalkoxyamine in a THF/isopropanol (isopropanol was chosen as the hydrogen donor compound) or *tert*-butylbenzene/isopropanol (when the reaction is performed at 90 °C) solution in which air was bubbling. The consumption of the starting PS-SG1 could be followed by EPR monitoring since each chain reacting leads to an increase of the SG1 concentration; nevertheless, EPR cannot be used to determine the degree of functionalization since side reactions like H atom transfer or alkyl radical coupling could not be taken into account. The ^{1}H NMR cannot be used as well because of the overlapping of the methylene protons bearing by the phosphoryl group (multiplet at δ = 3.8−4.5 ppm) of the SG1 with the methine proton neighboring the hydroxy chain end (δ = 4.2−4.5 ppm).

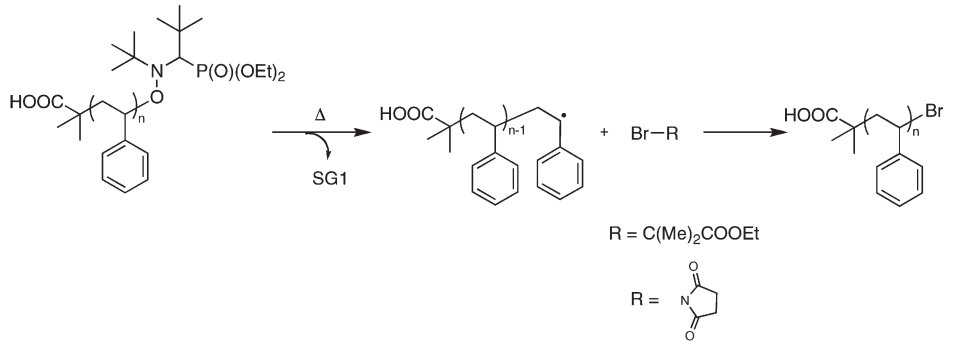
The reaction was then monitored by LC-CC which allows the separation of the polymer chains with respect to the chain end group. The effect of the temperature reaction on the reaction yield was investigated (Figure 2). The PS-OH prepared by nitroxide exchange was used in that case as a standard for the separation of end-capped polystyrenes. The analyses indicated that the reaction was quantitative when the experiment was performed at 90 °C overnight (Figure 2) whereas the PS-SG1 was not totally consumed for lower temperature, i.e., roughly 70 and 90% for 70 and 80 °C. Maldi-Tof analyses confirmed the hydroxylation of the polystyrene (see Supporting Information).

These results showed that hydroxy ω-functional polystyrenes were easily prepared by two different pathways: a two-step procedure consisting of an exchange with TEMPO nitroxide followed by a Zn/AcOH reduction reaction or via a one-pot procedure using the *in situ* preparation/reduction of the corresponding hydroperoxide.

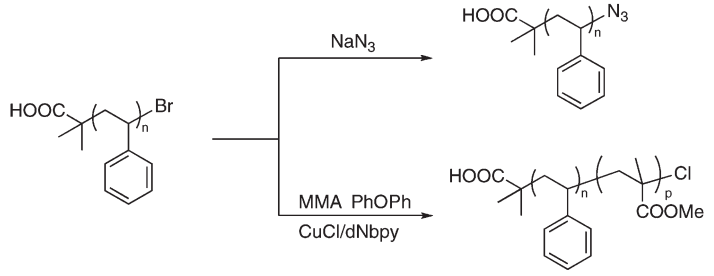
Radical Bromination. Since telechelic polymers can be easily prepared upon reaction of a halide end group with a

Scheme 3. (a) Radical Bromination Reaction and (b) PS-Br Postfunctionalization Reaction

a) Radical bromination reaction.



b) PS-Br post-functionalization reaction.



wide range of nucleophilic reagents, it is therefore highly desirable to replace the SG1 moiety by a bromide or a chloride atom. Moreover, this chemical transformation could also be used to combine the advantages of ATRP and NMP in a similar manner as Bon and Haddleton[63] did for ATRP and RAFT. Free radical halogenation and in particular bromination is a well-known radical reaction which is based on the use of bromine Br_2, carbon tetrabromide CBr_4, or *N*-bromosuccinimide NBS as versatile sources of bromine atom. In our case, we expected that the alkyl macroradicals produced upon the homolysis of PS-SG1 could abstract a bromine atom, leading to the corresponding PS-Br (Scheme 3a).

In a first series of experiments, we tried the bromination of PS-SG1 in the presence of *N*-bromosuccinimide as bromine transfer agent. The latter has been chosen since it is easier and safer to handle than Br_2 or CBr_4. Typically, a solution of PS-SG1 and 20 equiv of NBS in *tert*-butylbenzene were heated at 90 °C overnight. Compared to the starting material, even if the LC-CC analysis (Figure 3) of the obtained product showed a shift of the chromatogram peaks, the Maldi-Tof analysis and ^{1}H NMR spectrum were not consistent with a successful bromination reaction. The initial PS-SG1 was totally consumed, but the LC-CC chromatogram of the latter compound (Figure 3) was similar to the one obtained from the nonfunctional PS obtained after thiophenol reduction.

Therefore, we focused our attention on alternative routes in order to achieve this radical bromination. Zard et al.[64] studied the mild exchange reaction between xanthates and bromine. They found[64] that classical bromination reagents like bromotrichloromethane lead to complex mixtures with poor isolated yields. On the other hand, they showed that ethyl 2-bromoisobutyrate (EBiB) was an efficient bromine transfer agent under mild conditions. The success of this procedure is related to the high stabilization of the alkyl radical obtained after the loss of the bromine atom during the reaction. We extrapolated this methodology to replace

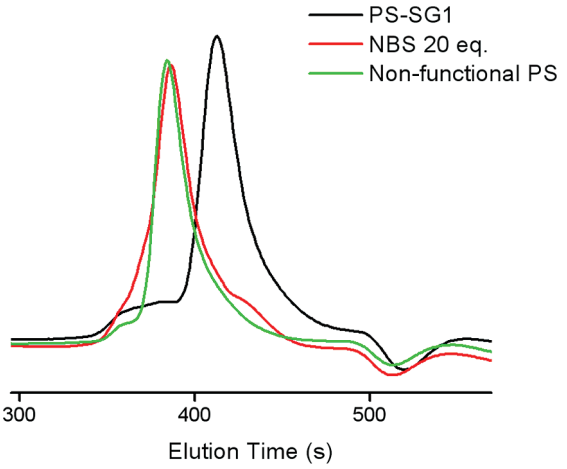


Figure 3. LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the bromination reaction using *N*-bromosuccinimide (NBS) as bromine transfer agent.

the SG1 moiety by a bromine atom on PS-SG1 chains. The reaction was conducted by heating PS-SG1 in ethyl 2-bromoisobutyrate, chosen as well as bromine transfer agent and solvent. It has to be noted that Zard et al.[64] used only a 5-fold excess of EBiB compared to the xanthate, but in our case the generated radicals are more stabilized than the ones used by Zard. Therefore, we decided to favor the reaction by increasing the concentration of the transfer agent.

The reaction was monitored by LC-CC, and the influence of the experimental conditions (temperature and duration of the experiment) on the reaction yield was examined. As the transfer reaction seemed to occur slowly, the reaction carried out at 85 °C presented a shoulder at lower retention times, corresponding to possible recombination products. When the temperature was lowered to 75 °C, this shoulder disappeared but the starting PS-SG1 was not totally consumed. The best results were obtained when the reaction was performed at

75 °C for 6 days. In that case the chromatogram showed a nearly quantitative shift of the peak corresponding to the macroalkoxyamine toward lower retention time, that is, toward another more polar species (Figure 4). The reaction should also lead to the synthesis of low molecular weight alkoxyamine ethyl isobutyrate-SG1. Nevertheless, at the reaction temperature, this product is not stable enough (it starts to decompose in solution at 30 °C) to isolate it after the completion of the reaction.

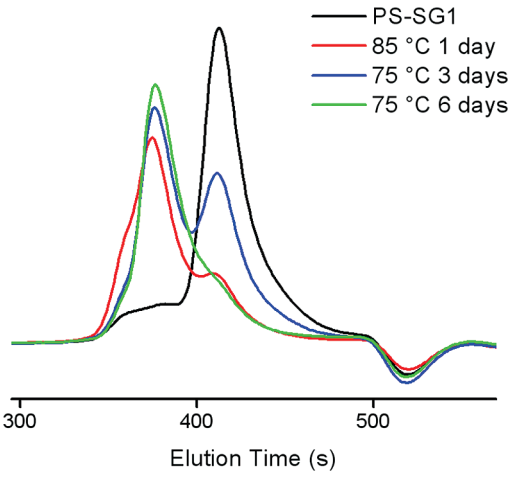


Figure 4. LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the bromination reaction using ethyl 2-bromoisobutyrate as bromine transfer agent.

The obtained polymer appeared to be more polar than the non-end-functional PS and less polar than the PS-OH, which is in accordance with the polarity of the bromine group.[65] The Maldi-Tof spectrum (see Supporting Information) as already noticed in the literature did not showed the desired end group but presented different populations with the major one having a terminal double bond.[60,66] Therefore, the qualitative identification of the bromine end group was further investigated by reacting the supposed PS-Br with sodium azide by the already described[67−69] nucleophilic substitution. The recorded LC-CC chromatogram was unexpected since no shift of the peak was observed (Figure 5a).

The polarity and therefore the interaction of these functional groups with the stationary phase should lead to different elution times. A thorough analysis of the literature data showed that similar results using gradient polymer elution chromatography (GPEC) have been already observed[70] for the transformation of dibromo PS to diazide PS. In that case the LC-CC could not be used, and the polymer was then analyzed by IR and ^{1}H NMR. The appearance of a narrow absorption band at 2093 cm^{-1} (Figure 5b) characteristic of the alkyl azide group was observed. The ^{1}H NMR spectrum

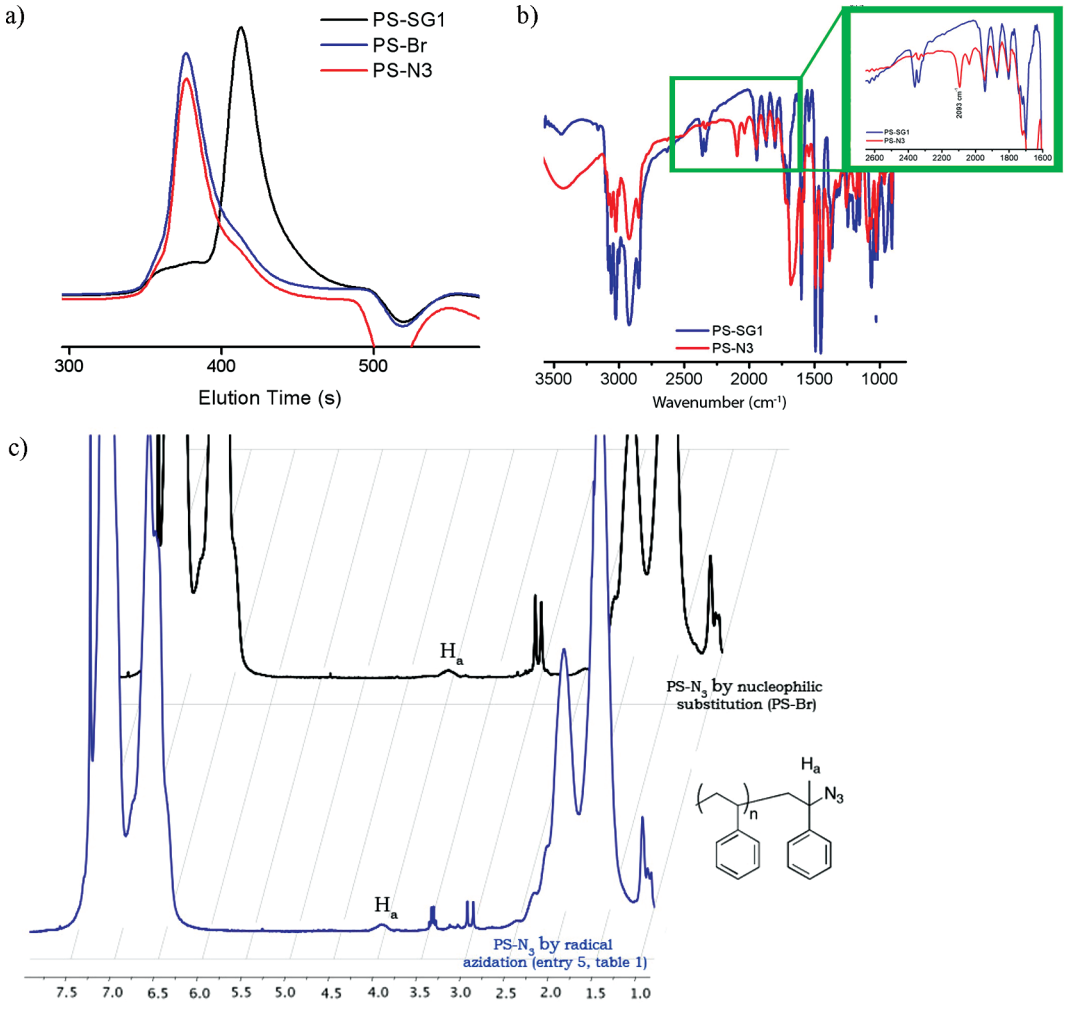


Figure 5. (a) LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the nucleophilic azidation reaction. (b) Comparison of the IR spectra of the PS-SG1 and PS-N_3 obtained after radical bromination followed by nucleophilic azidation reaction. (c) ^{1}H NMR spectra of PS-N3 obtained either by radical azidation or by nucleophilic substitution of the PS-Br intermediate.

represented in Figure 5c showed the characteristic signal from 3.8 to 4.1 ppm due to the methine proton neighboring the azide chain end.[67] The integration of this signal and the signal of the polymer backbone led to 73% of functionalization. The Maldi-Tof spectrum (Supporting Information) presented three populations: one with the desired end group (129 g mol^{-1}) and two other populations corresponding to the loss of N_2 and N_3 as already reported by Matyjaszewski.[68] Therefore, the Maldi-Tof confirmed the successful chemical modification of the PS-Br.

To illustrate further the interest of the bromination reaction, we coupled the functionalization reaction with ATRP to combine the advantages of the two CRP techniques. As the main drawback of NMP using SG1 is the uncontrolled polymerization of the pure methacrylate derivatives,[71] we aimed to prepare a PS-*b*-PMMA block copolymer to prove the utility of this functionalization. The synthesis of such copolymers by successive ATRP is not straightforward since the apparent rate constant of initiation is lower than the one of propagation.[72] This leads to an inefficient extension of the macroinitiator and a product with a multimodal distribution of molecular weights. A procedure was then developed to overcome this problem. The halogen exchange method, using a bromide-terminated initiator in conjunction with a CuCl-based catalyst complex, allowed to prepare relatively well-defined copolymers even if there is an increase of the PDI.[72]

We therefore used the procedure described by Matyjaszewski[72] to prepare such a copolymer. The polymerization at 90 °C for 18 h in diphenyl ether (1:1 v:v) using CuCl/dNbpy leaded (Figure 6a) to 89% of conversion, and the M_n increased from 4900 g mol^{-1} (PDI = 1.2) to 22 000 g mol^{-1} (PDI = 1.4). The experimental and theoretical M_ns (22 700 g mol^{-1} for 4900 + 20000 × conversion) are in good agreement, suggesting a good reinitiation efficiency.

The increased PDI and the chromatogram after reinitiation presented nevertheless a tail toward lower retention time characteristic of a relatively slow initiation inherent to the system. LC-CC at the critical condition for the PS block was also performed, and a clear shift of the diblock peak is observed (Figure 6b). A tail toward less polar species is present, characteristic of different lengths of PMMA due to the slow initiation; nevertheless, no clear peak related to unreacted PS was observed. All the characterization techniques showed therefore that the radical bromination allowed an efficient functionalization and that the combination of NMP and ATRP is now possible.

Radical Azidation. Click chemistry and specially copper-catalyzed azide−alkyne cycloaddition first described in 2001 by Sharpless et al.[73] have been the object of intensive research in polymer science because it is a very useful and versatile toolbox to prepare macromolecular complex architectures. Since Matyjaszewski et al.[68,69] showed that polymers prepared by ATRP could be easily functionalized by an azide group, numerous authors have used this reactivity to prepare multisegmented,[74−76] cyclic,[77,78] functional,[67,79,80] or bioconjugated polymers.[81−83] It is therefore highly valuable to develop a procedure to prepare chain end azide-functionalized polymers that were previously made by NMP.

As for the hydroxy functionalization, the azidation functionalization could be obtained as described above is a two-step procedure after the preparation of a PS-Br precursor. Since multistep chemical modification on macromolecules could be the source of different problems (purification, cost, etc.), we decided to focus our attention on the preparation of azide-functionalized polymers using a one-step straightforward procedure. For that purpose, we extrapolate to macromolecules the recent work of Renaud,[49,84,85] who showed

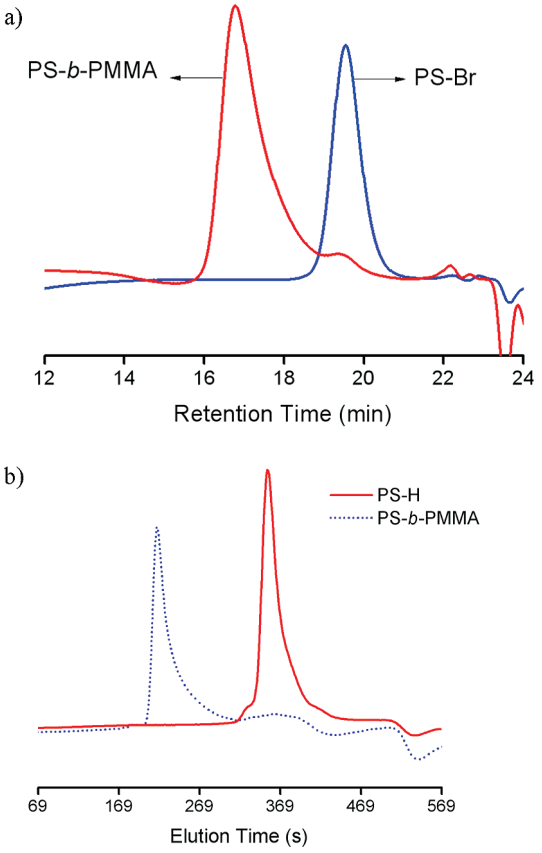


Figure 6. (a) Comparison of the SEC chromatograms before and after the polymerization of methyl methacrylate at 90 °C in diphenyl ether (1:1 v:v) using CuCl/dNbpy as catalytic system. (b) Comparison of the LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the diblock copolymer and a non-end-functionalized PS.

that radical azidation could be performed using alkanesulfonyl azide (Scheme 4).

In this process, the alkyl radical adds to the γ-position of the azido moiety to give the 1,3-triazenyl radical.[86] This radical rapidly undergoes fragmentation to generate the desired alkyl azide and the unstable ethanesulfonyl radical, which affords after sulfur dioxide expulsion the ethyl radical. The application of this radical azidation process to various substrates[84,87,88] highlighted the low reactivity of alkyanesulfonyl azide as a carbon-centered radical trap. For example, the addition of electrophilic radical is extremely slow due to the high electrophilicity of the radical trap. Very recently, Braslau et al.[89] used the same approach to functionalize TIPNO-based polystyrenes. The reaction was performed at 120 °C for 4 h with 5−10 equiv of $EtSO_2N_3$ and lead to less than 30% of chemical modification.

The polystyryl macroradical is not a strong electrophilic radical, but to favor the azidation reaction, we carried out the experiments with an excess of ethanesulfonyl azide. We also studied both the effect of the temperature and the ratio between the azidation reactant and the polymer (Figure 7a and Table 1) on the efficiency of the reaction. The LC-CC analysis showed in all cases a shift to more polar species and a similar elution volume as the PS-N_3 prepared following the two-step procedure. The reaction yield was monitored by ^1H NMR (the methine proton neighboring the azide group; see Figure 5c) as already done by Lutz et al.[67]

When the reaction was performed with a low $[EtSO_2N_3]_0/[PS\text{-}SG1]_0$ ratio (entries 1 and 2, Table 1), the LC-CC chromatogram presented an important shoulder to

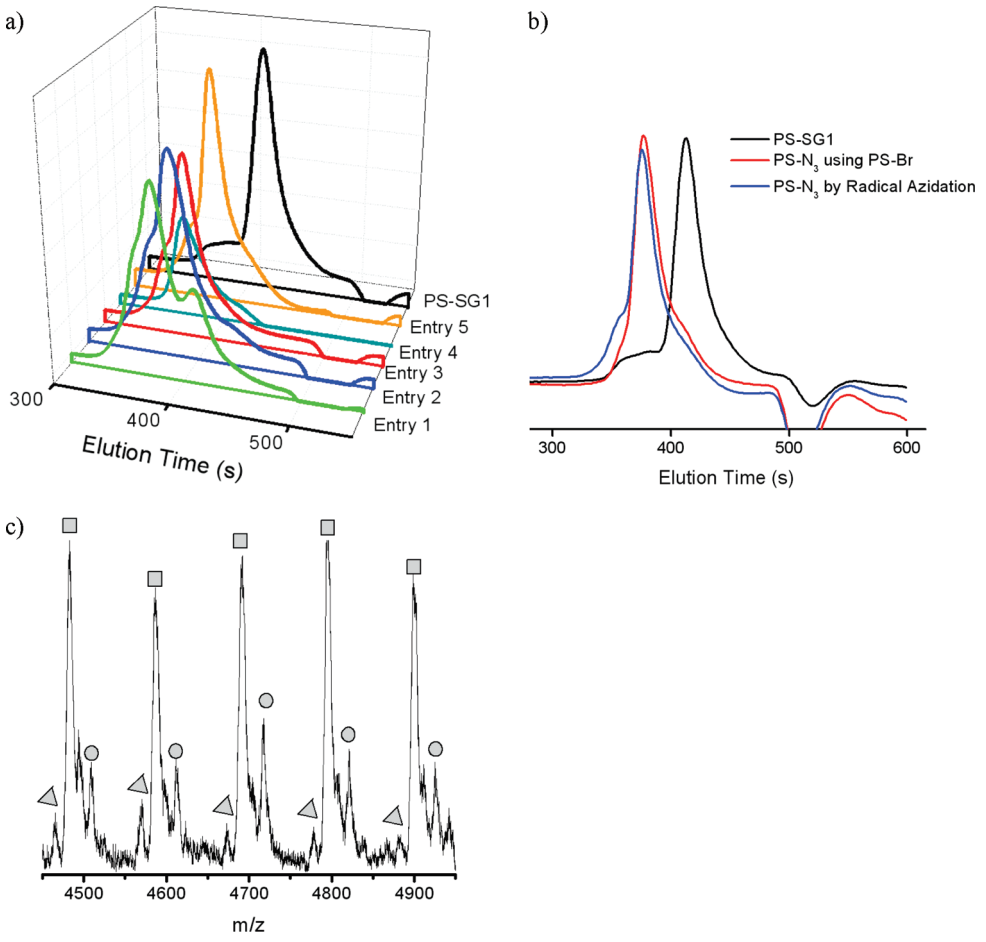


Figure 7. (a) LC-CC chromatogram (DMF, 82.5 °C, C18 nucleodur columns) of the radical azidation reaction. Optimization of the experimental conditions (see Table 1 for details). (b) Comparison of LC-CC chromatograms obtained by radical and nucleophic azidation reaction. (c) Maldi-Tof analysis of radical azidation reaction. Three populations could be observed: (△) $m/z = 87.01 + n \times 104.15 + 1$ (H) (+ 107.86 Ag^+) g mol^{-1} loss of N_3; (□) $87.01 + n \times 104.15 + 17$ (NH_2) (+ 107.86 Ag^+) g mol^{-1} loss of N_2; (○) $m/z = 87.01 + n \times 104.15 + 42$ (N_3) (+ 107.86 Ag^+) g mol^{-1}.

Scheme 4. Radical Azidation Reaction

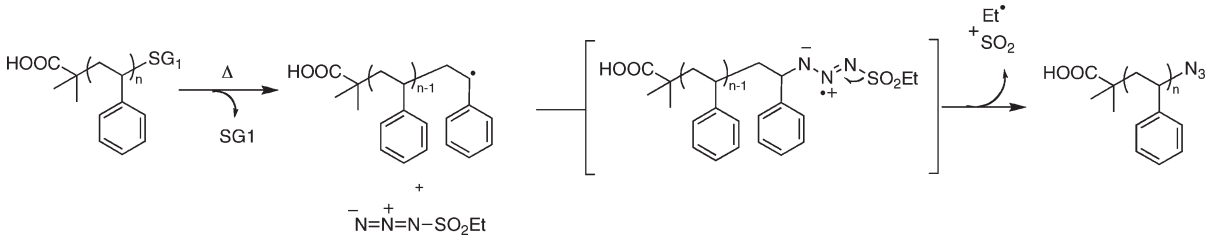


Table 1. Experimental Conditions Used for the Radical Azidation Reaction

entry	temp/°C	$[EtSO_2N_3]_0/[PS\text{-}SG1]_0$	solvent	duration	yield[a]/%
1	120	10	*tert*-butylbenzene	16 h	[b]
2	100	20	*tert*-butylbenzene	2 days	35
3	90	50	DMF	3 days	62
4	80	50	DMF	5 days	45
5	90	350	DMF	3 days	57

[a] Determined by the relative integration of the signal at 3.8−4.1 ppm and the signal of the polymer backbone. [b] Not determined since there was some unreacted PS-SG1 whose signal (3.8−4.5 ppm) overlapped with the PS-N_3.

both higher and lower retention time indicating of a non-negligible occurrence of side reactions. To balance the low reactivity of ethanesulfonylazide as radical trap, we increased the $[EtSO_2N_3]_0/[PS\text{-}SG1]_0$ ratio, decreased the reaction temperature to lower the instantaneous macroradical concentration, and performed the reactions in a more polar solvent (DMF). In these conditions narrower chromatograms were observed. The best reaction condition reactions were found to be 90 °C for 3 days with 50 equiv of ethanesulfonyl azide for 1 equiv of PS-SG1 (Figure 7b). Adding more azidation reagent did not lead to an increase of the reaction yield. In that case the elution peaks of PS-N_3 obtained by radical azidation and nucleophilic substitution are quite similar, indicating that a large majority of the chains are azide-terminated. This result

showed that a good azide functionalization (up to 70%) could be obtained using optimized conditions (relatively low temperature 90 °C and a large amount of $EtSO_2N_3$).

In that case, the Maldi-Tof spectrum (Figure 7c) was in agreement with the azide-terminated PS structure[68] and similar to the one we obtained after the two-step procedure (see Supporting Information). The IR spectrum (see Supporting Information) of this polymer presented a low-intensity band at 2140 cm^{-1} (characteristic of residual $EtSO_2N_3$) and at 2093 cm^{-1}, similar to the one obtained in Figure 5b, characteristic of the azide group. These results showed that the radical azidation of PS-SG1 could be performed in one step using ethanesulfonyl azide.

Conclusions

Polymers prepared by NMP using the highly hindered SG1 nitroxide were end-functionalized using radical reactions since the classical methods used with TEMPO or TIPNO were unsuccessful. Hydroxy-functional polystyrenes could be prepared easily from a polystyrene-SG1 precursor. Two different radical reactions have been performed using either an optimized exchange with TEMPO nitroxide followed by a Zn/AcOH reduction or a straightforward radical hydroxylation. In both cases, the reaction was monitored by liquid chromatography at the critical condition in pure eluent. Quasi-quantitative functionalization occurred for both reactions. In a similar approach, azide-functional polystyrene with a yield close to 70% could be also prepared either by a radical azidation reaction using ethanesulfonyl azide or by a two-step procedure using a PS-Br as intermediates. This PS-Br was obtained by a mild radical bromination reaction using ethyl 2-bromoisobutyrate as bromine transfer agent. The transformation of the nitroxide moiety to a bromine end group both opens the range of the complex architecture available using the combination of NMP and ATRP and opens also the range of chemical postmodification used in ATRP for polymer prepared by NMP.

This work demonstrates that end-functionalization is not anymore a technological barrier for SG1-mediated polymerization. Furthermore, since these reactions are radical reactions, they could be extrapolated to other nitroxides as control agents or other polymers prepared by different CRP techniques.

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Supporting Information Available: Maldi-Tof spectra of PS-OH obtained by hydroxylation reaction and PS-N_3 obtained by both radical bromination followed by nucleophilic substitution and radical azidation; IR spectra of PS-SG1 and PS-N_3 obtained after either radical azidation reaction or nucleophilic substitution. This material is available free of charge via the Internet at http://pubs.acs.org.

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