Improving the Control of Styrene Polymerization at 60 °C Using a Dialkylated α-Hydrogenated Nitroxide

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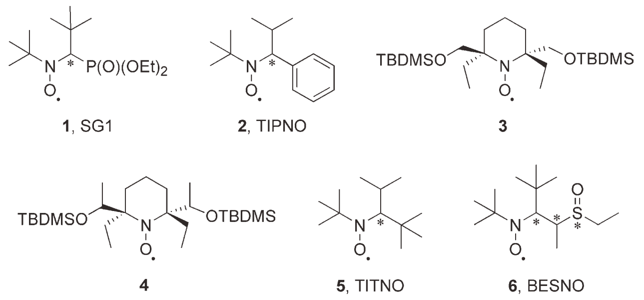
ABSTRACT: A new dialkylated α-hydrogenated linear nitroxide and the corresponding 1-phenylethyl alkoxyamine were synthesized in two and three steps, respectively. The alkoxyamine was involved in the polymerization of styrene at 60 °C, and the *in situ* concentration of nitroxide was monitored by electron spin resonance spectroscopy. The enhanced characteristics of these new alkylated alkoxyamine and nitroxide ($k_d^{60} = 1.5 \times 10^{-4}$ s^{-1} and $k_c^{60} = 5.7 \times 10^{4}$ L mol^{-1} s^{-1}) yielded a monomer consumption one order of magnitude higher than styrene thermal polymerization. This resulted in well-defined polystyrenes up to 70,000 g mol^{-1} and the observation of a control occurring through the establishment of the radical persistent effect, that is, $\ln([M]_0/[M]) = t^{2/3}$. Experimentally determined kinetic constants were involved in PREDICI modelings to investigate the influence of temperature and initial alkoxyamine concentration on the kinetics as well as on the livingness and the controlled character of the polymerization. © 2012 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 000: 000–000, 2012

KEYWORDS: alkoxyamine; kinetics (polym.); nitroxide mediated polymerization (NMP); polystyrene; radical polymerization; styrene

INTRODUCTION With the development of controlled and/or living radical polymerization (CLRP) techniques, the versatile control of the structure and architecture of vinyl polymers that exhibit specific properties and functionalities is now well established.[1] Although nitroxide mediated polymerization (NMP) has been the first CLRP method to be developed, atom transfer radical polymerization (ATRP)[2,3] and reversible addition/fragmentation chain transfer (RAFT) polymerization[4–6] have rapidly demonstrated interesting advantages and improved efficiencies such as a wider range of controllable monomers, lower polymerization temperatures, and a broader combination with robust, efficient, and orthogonal chemistries.[1,7–10] However, NMP is one of the simplest method to implement due to its thermally activated monocomponent control system and a simple purification process based on precipitation to remove monomer residuals. These features, together with the absence of cytotoxicity for nitroxides, alkoxyamines and polymers made by this method,[11] have always clearly represented unquestionable advantages of NMP over other CLRP techniques.[12,13] In addition, in the last 15 years, significant efforts have allowed the main weaknesses of NMP to be efficiently solved, or at least significantly lowered[12] as for instance the range of monomers[14–19] or the range of macromolecular architecture[20–23] that has been significantly extended. In particular, the use of additives to enhance the rate of polymerization,[24,25] the design of highly labile alkoxyamines based on highly crowded alkyl moieties,[26] and the design of new nitroxides with enhanced structural features[12] afforded a substantial decrease of the polymerization temperature. For instance, *N-tert*-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide (**1** or SG1, Scheme 1)[27] and 2,2,5-trimethyl-4-phenyl-3-azahexane-3-oxyl nitroxide (**2** or TIPNO)[28] were shown to have the best balance between their efficiency, their good thermal stability at elevated temperatures and a moderate difficulty for their synthesis. Few other structures such as hindered cyclic nitroxides prepared by Studer et al. (**3**,**4**) are very efficient since the successful polymerization of styrene and *n*-butyl acrylate

Additional Supporting Information may be found in the online version of this article.



SCHEME 1 Chemical structures of nitroxides **1-6**.

could be performed between 70 and 90 °C.[29,30] Nevertheless, the preparation of such nitroxides and the corresponding alkoxyamines requires demanding multistep synthetic procedures.[29,30] More recently, Cameron et al.[31] patented the controlled polymerization of styrene at 60 °C using *N-tert*-butyl-*N*-(1-*tert*-butyl-2-methyl)propyl nitroxide (**5**). However, additional data regarding nitroxide's stability, accurate determination of kinetic parameters, and extension to the preparation of high molar mass polymers would precise the real potential of this promising persistent radical.

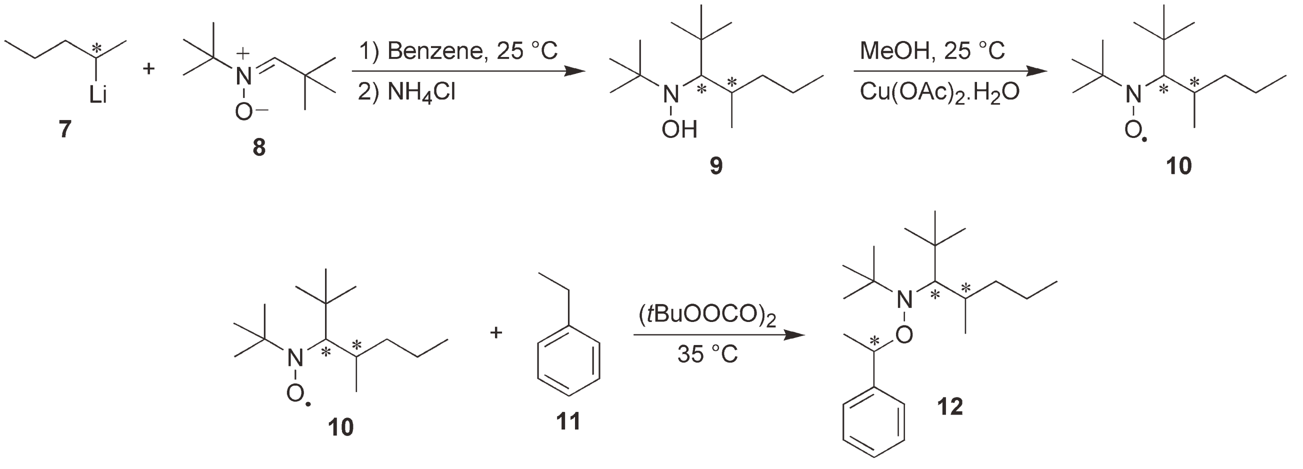
Besides, one diastereomer mixture ($R_SR_\beta R_\alpha/S_SS_\beta S_\alpha$) of *N-tert*-butyl-*N*-(1-*tert*-butyl-2-ethylsulfinylpropyl) nitroxide (**6** or BESNO), a chiral *β*-sulfinyl nitroxide developed by Catala et al. was shown to efficiently control the polymerization of ethyl acrylate, *n*-butyl acrylate and styrene below 90 °C,[32–34] showing in the case of styrene a rate of polymerization significantly higher than the rate of thermal polymerization.[33,35] Conversely, the other BESNO diastereomers ($S_SR_\beta R_\alpha/R_SS_\beta S_\alpha$) were not able to control the polymerization of acrylates and the control of styrene polymerization was only possible at temperatures above 110 °C with a rate of polymerization comparable to thermal polymerization of styrene. Although the rate constant of combination (k_c) was found independent of the BESNO stereochemistry, a one order of magnitude difference was observed for the rate constant of dissociation (k_d) of the different diastereomer mixtures of the corresponding 1-phenylethyl alkoxyamines.[32] This particular behavior stems from the different orientation of the strongly polar sulfoxide functionality with respect to the nitroxide moiety induced by the stereochemistry of the persistent radical. This characteristic requires, therefore, the separation of diastereomers and thus complicates the large scale preparation of this specific mixture of diastereomers. The peculiar skeleton of BESNO nitroxide is nevertheless highly interesting and the aim of this article is to investigate the replacement of the sulfoxide group by a methylene group and its impact on the properties of the resulting 1-phenylethyl alkoxyamine with respect to stereochemistry. We report herein the electron spin resonance (ESR) spectroscopy and kinetic studies of the polymerization of styrene at 60 °C mediated by the 1-phenylethyl alkoxyamine of this new alkylated analogue of BESNO. PREDICI modelings using the kinetic rate constants determined experimentally herein were performed to explore the influence of various parameters such as conversion, temperature, and initial alkoxyamine concentration on the livingness and the controlled character of the polymerization of styrene.

RESULTS AND DISCUSSION

Synthesis

Nitroxide **10** was synthesized in two steps, taking advantage of the high reactivity of nitrones toward nucleophiles, and the mild oxidation of the resulting hydroxylamine to afford the corresponding nitroxide functionality (Scheme 2). This versatile two-step strategy is particularly efficient and requires fewer synthetic and purification steps compared to nitroxides previously shown to control the polymerization of styrene at moderate temperatures such as nitroxides **3**, **4,** or **6**.[29,30,32]

The nucleophilic addition of *sec*-pentyllithium **7** to *N-tert*-butyl-*α*-*tert*-butyl nitrone **8** was performed at room temperature, thus affording all possible diastereomers of hydroxylamine **9** (i.e., $S_\alpha R_\beta/R_\alpha S_\beta$ and $R_\alpha R_\beta/S_\alpha S_\beta$) in 70% yield. Subsequent mild oxidation of the hydroxylamine intermediate by copper(II) acetate monohydrate afforded quantitatively nitroxide **10**, a *per*-alkylated analog of nitroxide **6**. Conversely to



SCHEME 2 Synthesis of nitroxide **10** and the corresponding 1-phenylethyl alkoxyamine **12**.

strongly polar BESNO nitroxide **6** ($a_N = 14.7$ G for $S_SR_\beta R_\alpha$/$R_SS_\beta S_\alpha$ and $a_N = 13.6$ G for $R_SR_\beta R_\alpha$/$S_SS_\beta S_\alpha$ diastereomers), the different diastereomers involved in the composition of nitroxide **10** are characterized by identical values of the nitrogen hyperfine coupling constant ($a_N = 13.6$ G). It is worth mentioning that this a_N value matches the one observed for the diastereomer mixture of BESNO nitroxide able to control the polymerization of acrylates and styrene significantly above the rate of thermal polymerization at temperatures below 90 °C. As observed previously, the hyperfin coupling of the spin radical with the β-hydrogen atom (a_H) was not observed on the ESR spectra (Fig. S1 in the Supporting Information). Indeed, the steric hindrance of the α-*tert*-butyl substituent stabilizes the conformations where the β-hydrogen and the nitroxide functionality do not interact. It was verified by ESR spectroscopy that nitroxide **10** is extremely stable in benzene at elevated temperatures (Fig. S2 in the Supporting Information).

Alkoxyamine **12** was then synthesized from the coupling of nitroxide **10** diastereomers with 1-phenylethyl radicals issued from the decomposition of di-*tert*-butyl peroxalate in ethylbenzene **11** at 35 °C (Scheme 2). This particular reaction allowed working at rather low temperature, which is mandatory regarding the fast dissociation of the resulting alkoxyamine. However, other mild methods for alkoxyamine preparation such as atom transfer radical addition or photochemical alternatives could be used.[36–41] Even not structurally resolved, two diastereomer mixtures of alkoxyamine **12** were partially isolated by column chromatography and their k_d values determined at 60 °C in benzene by ESR spectroscopy using a previously reported protocol based on galvinoxyl as spin trap.[32,33] Conversely to BESNO analogs, and consequently to the absence of strong dipole moment, the distinct stereochemistry of the nitroxide moiety did not induce any significant difference in the k_d values of the different alkoxyamine diastereomers. Compared to sulfoxide-functionalized diastereomers of nitroxide **6**, this alkylated alkoxyamine does not require tedious separation of diastereomers with distinct properties, thus contributing to the versatile nature of the synthetic approach developed herein. Therefore, the crude diastereomer mixture of alkoxyamine **12** was involved in subsequent ESR and polymerization experiments.

ESR and Polymerization Kinetics

The accurate determination of k_d by ESR spectroscopy experiments performed at temperatures ranging from 70 to 90 °C (Fig. S3 in the Supporting Information), yielded the following Arrhenius parameters: $A = 1.8 \times 10^{14}$ s^{-1} and $E_a = 115 \pm 2$ kJ mol^{-1} (Fig. S4 in the Supporting Information). As it could be expected from the ESR parameters (i.e., a_N and g), the values obtained for the activation energy (E_a/kJ mol^{-1}) and the frequency parameter (A/s^{-1}) are similar to those determined for the $R_SR_\beta R_\alpha$/$S_SS_\beta S_\alpha$ BESNO-1-phenylethyl alkoxyamine and are in agreement with the general frequency parameter ($A = 2.4\ 10^{14}$ s^{-1}) determined by Marque and coworkers[42] for several tailor-made alkoxyamines. Indeed, the main parameter generally involved in the C—O bond homolysis is the steric hindrance of both the transient and persistent radical moieties. For the other BESNO diastereomers ($S_SR_\beta R_\alpha$/$R_SS_\beta S_\alpha$), the dipole interaction of the sulfoxide moiety with the *N*-oxyl radical is marked by an increase in the nitrogen hyperfine coupling constant ($a_N = 14.7$ G) and a decrease in k_d.

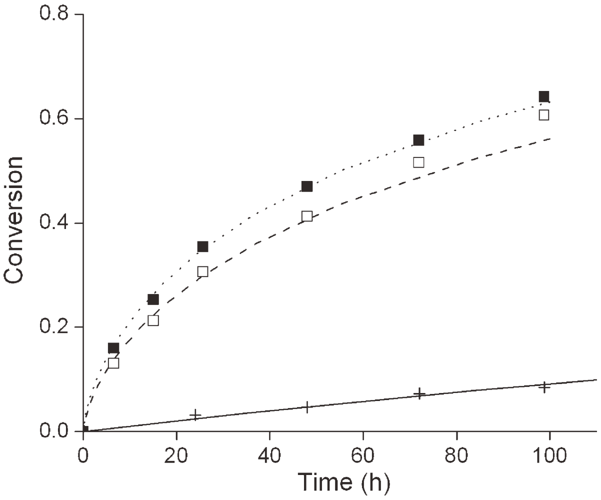


FIGURE 1 Monomer conversion versus time for the bulk polymerization of styrene at 60 °C: (+, solid line) thermal polymerization of neat styrene; (■, dotted line) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□, dashed line) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (solid, dotted and dashed lines) PREDICI modelings.

The particularly fast dissociation of alkoxyamine **12** at 60 °C ($k_d^{60} = 1.5 \times 10^{-4}$ s^{-1}, $t_{1/2}^{60} = 4621$ s) prompted us to study the bulk polymerization of styrene at this temperature. Two alkoxyamine concentrations ($[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1} and 14.2×10^{-3} mol L^{-1}) were used to investigate the effect of the initial alkoxyamine concentration on the rate of polymerization as well as the possibility to reach high molar mass polystyrenes. The *in situ* evolution of nitroxide concentration for each polymerization experiment was also monitored by ESR spectroscopy. Interestingly, the evolution of monomer conversion with time (Fig. 1) reveals a rate of polymerization about one order of magnitude higher than styrene thermal polymerization and that depends on the initial alkoxyamine concentration $[\mathbf{12}]_0$.

As expected for the highest initial alkoxyamine concentration ($[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}, i.e., $M_{n,th} = 65{,}000$ g mol^{-1}) the number average molar mass (M_n) increases linearly with conversion in perfect agreement with theoretical values and dispersity ($Đ$) reaches values close to 1.1 (Figs. 2 and 3, respectively). For the lowest initial alkoxyamine concentration ($[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}, i.e., $M_{n,th} = 112{,}500$ g mol^{-1}) a similar trend was observed that is more surprising since it is known that obtaining $M_n > 50{,}000$ g mol^{-1} with $Đ$ below 1.2 is very challenging.[25] Such noteworthy experimental observations led us to investigate deeper the kinetics involved in this system.

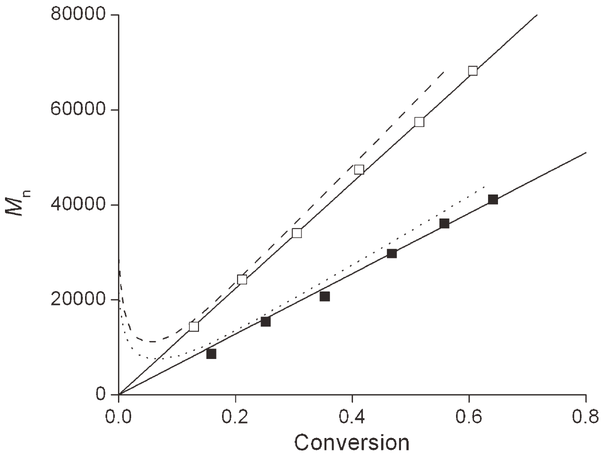


FIGURE 2 Number average molar mass (M_n) versus monomer conversion for the bulk polymerization of styrene at 60 °C in the presence of alkoxyamine **12**: (solid lines) theoretical M_n values; (■, dotted line) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□, dashed line) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (dotted and dashed lines) PREDICI modelings.

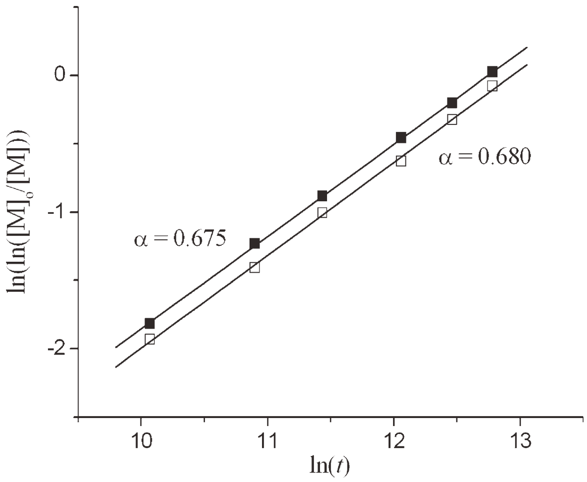


FIGURE 4 Double logarithmic plot of conversion index versus time for the bulk polymerization of styrene at 60 °C in the presence of alkoxyamine **12**: (■) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (solid lines) linear fits.

For highly labile alkoxyamines, there is a constant debate regarding the mechanism that governs the control of the polymerization (i.e., by the persistent radical effect and then the plot of conversion index versus time$^{2/3}$ should be linear or by a reversible termination process and then the plot of conversion index versus time should be linear).[26] This question was assessed by plotting the double logarithmic plot of conversion index versus time (Fig. 4). The slopes obtained for both initial alkoxyamine concentrations are extremely close to 2/3, characteristic of a polymerization controlled by the persistent radical effect. It is worth mentioning that such an ideal persistent radical effect has been scarcely experimentally observed[26,43] earlier in the case of styrene as a consequence of the significant additional source of transient radicals issued from the thermal polymerization of styrene, that is, when monomer conversion is comparable to thermal polymerization of styrene as generally observed for previously reported alkoxyamines.[44,45]

This particular evolution of monomer conversion in the case of styrene NMP is correlated to the steady increase of nitroxide concentration ([**10**]), which follows a $t^{1/3}$ dependence (Fig. 5) as expected from the persistent radical effect mechanism.

Equations 1 and 2 describe the theoretical time dependence of [**10**] and $\ln([M]_0/[M])$ as established by both Fischer and Fukuda.[46,47] However, both equations rely on the k_c between nitroxide **10** and 1-phenylethyl transient radicals as well as

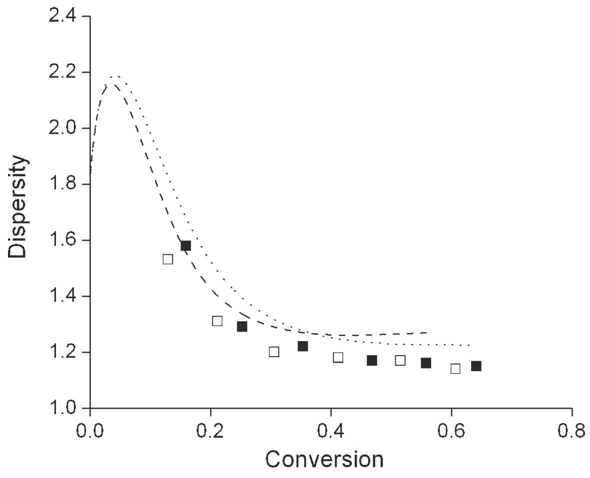


FIGURE 3 Evolution of dispersity (*Đ*) with monomer conversion for the bulk polymerization of styrene at 60 °C in the presence of alkoxyamine **12**: (■, dotted line) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□, dashed line); $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (dotted and dashed lines) PREDICI modelings.

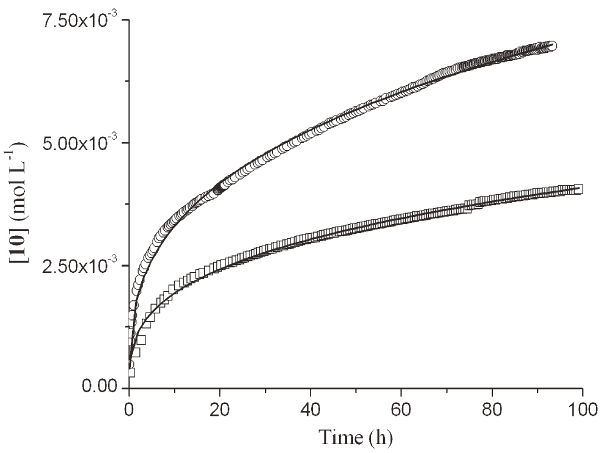


FIGURE 5 Evolution of nitroxide **10** concentration as a function of time for the bulk polymerization of styrene at 60 °C in the presence of alkoxyamine **12**: (○) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (solid lines) $t^{1/3}$ fit of the experimental data.

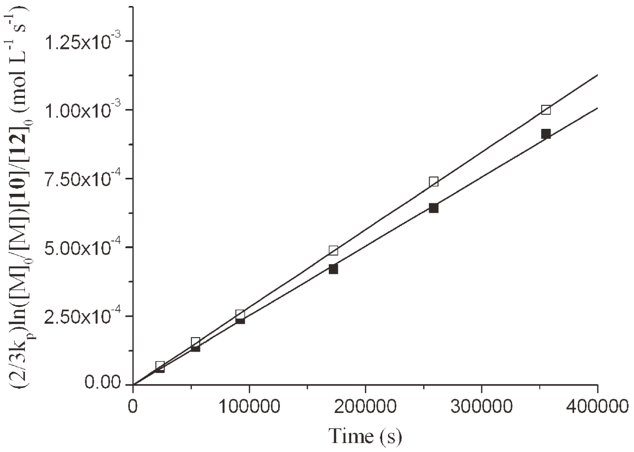


FIGURE 6 Determination of the equilibrium constant (K^{60}) for the bulk polymerization of styrene at 60 °C in the presence of alkoxyamine **12**: (■) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (□) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (solid lines) linear fits.

on the termination rate constant (k_t) of styrene. This former value is not accurately established throughout the polymerization. Therefore, the equilibrium constant (K) could be determined using eq 3, a combination of eqs 1 and 2 that is independent of k_t:

$$[\mathbf{10}] = \left(\frac{3k_t k_d^2[\mathbf{12}]_0^2}{k_c^2}\right)^{1/3} t^{1/3} \tag{1}$$

$$\ln\frac{[M]_0}{[M]} = \frac{3k_p}{2}\left(\frac{k_d[\mathbf{12}]_0}{3k_t k_c}\right)^{1/3} t^{1/3} \tag{2}$$

$$\frac{2}{3k_p}\frac{[\mathbf{10}]\times\ln\frac{[M]_0}{[M]}}{[\mathbf{12}]_0} = K\times t \tag{3}$$

Relation 3 was thus plotted in Figure 6 using the experimental values of the conversion index, nitroxide concentration [**10**], initial alkoxyamine concentration $[\mathbf{12}]_0$, and the propagation rate constant (k_p) of styrene that has been accurately established earlier by the IUPAC subcommittee on polymerization kinetics.[48]

For each $[\mathbf{12}]_0$, the equilibrium constant (K^{60}) was then determined from the slopes of the resulting straight lines (Table 1). The high average value of the equilibrium constant ($K^{60} = 2.6 \times 10^{-9}$ mol L^{-1}) thus results from a high value of k_d^{60} (determined by ESR spectroscopy) and a particularly low value of k_c^{60} ($k_c^{60} = k_d^{60}/K^{60} = 5.7 \times 10^4$ L mol^{-1} s^{-1}).

This result is thus very interesting and in rather good agreement with the work of Siegenthaler and Studer[30] that already investigated the influence of the k_c value on the outcome of a NMP process. They concluded that the lower the k_c, the lower the temperature of polymerization at a given k_d value, but this is only true above a threshold value, after which a loss of control is obtained. Indeed for a given k_d, a lower k_c increases K, shifts the equilibrium toward active species and thus either increases the polymerization kinetics or allows the control of the polymerization at lower temperatures. Nevertheless, if the K value becomes too high, the nitroxide is not efficient enough to decrease the instantaneous macroradical concentration and the contribution of irreversible termination reactions improves significantly. That means that below a threshold value for k_c, it is not possible to obtain a controlled polymerization.

If nitroxides **6** and **10** are compared, their k_d are similar (i.e., 1.5×10^{-4} s^{-1} for **12** and 0.9×10^{-4} s^{-1} for BESNO-based 1-phenylethyl alkoxyamine) but k_c is one order of magnitude lower for **10** than for **6** leading to the possibility to decrease the reaction temperature with the same level of control. Moreover, k_c of nitroxide **10** with 1-phenylethyl radicals is two order of magnitude lower than TIPNO and such a decrease could be detrimental to the control as observed by Siegenthaler and Studer.[30] But concomitantly, the k_d value of **12** is one order of magnitude higher than the k_d of 1-phenylethyl-TIPNO alkoxyamine allowing to decrease the polymerization temperature since the decomposition of the (macro)-alkoxyamine remains significant. Thus, similar values of K (2.5×10^{-9} mol L^{-1} at 60 °C for **10** and close to 2.0×10^{-9} mol L^{-1} at 120 °C for TIPNO,[49]) are reached but at a much lower temperature in the case of **10**.

PREDICI Modelings

To investigate further the potential of nitroxide **10**, PREDICI modelings[50] were performed using a previously established model[26,51] and the kinetic rate constants (k_d and k_c) determined experimentally in this work. Indeed, PREDICI has previously described efficiently all CLRP techniques including NMP,[51] ATRP,[52] and RAFT polymerization.[53] The mechanism scheme and the kinetic rate constants used to model the polymerization of styrene mediated by alkoxyamine **12** are described in the Supporting Information section. As can be observed on Figures 1–3, the experimental data and the PREDICI modelings are in rather good agreement for the two $[\mathbf{12}]_0$ studied. Particularly, the evolutions of conversion versus time and molar mass versus conversion are extremely well described by the modelings on the whole range of conversion studied herein.

This rather good accordance between modelings and experimental results allowed the use of this model to investigate the livingness of the polymerization. As the living fraction (i.e., the ratio between alkoxyamine chains-ends and the total number of chains) strongly decreases with the increase in targeted molar mass,[51] a wide range of initial alkoxyamine concentrations ($[\mathbf{12}]_0$ ranging from 5.0×10^{-2} to $3.0 \times$

TABLE 1 Kinetic Parameters for the Bulk Polymerization of Styrene at 60 °C Mediated by Alkoxyamine **12**

$[\mathbf{12}]_0$ (mol L^{-1})	k_d^{60} (s^{-1})[a]	K^{60} (mol L^{-1})[b]	k_c^{60} (L mol^{-1} s^{-1})[c]
8.1×10^{-3}	1.5×10^{-4}	2.5×10^{-9}	6.0×10^4
14.2×10^{-3}	1.5×10^{-4}	2.8×10^{-9}	5.4×10^4

[a] Determined by ESR spectroscopy.
[b] Determined from relation 3.
[c] $k_c^{60} = k_d^{60}/K^{60}$.

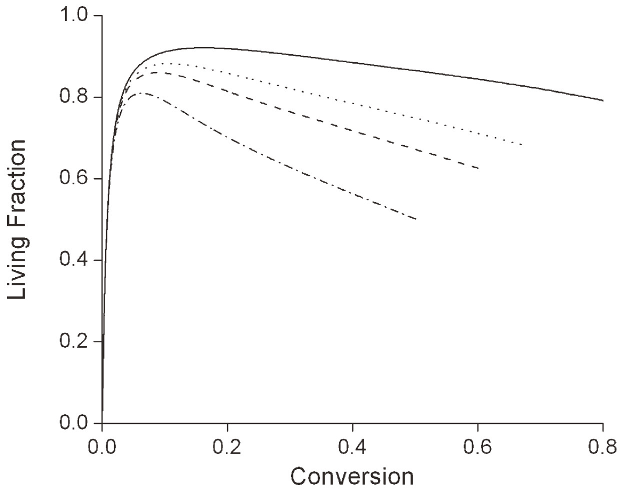


FIGURE 7 PREDICI modeling of the living fraction versus monomer conversion for the bulk polymerization of styrene at 60 °C at different $[\mathbf{12}]_0$: (solid line) $[\mathbf{12}]_0 = 5.0 \times 10^{-2}$ mol L^{-1}; (dotted line) $[\mathbf{12}]_0 = 8.1 \times 10^{-3}$ mol L^{-1}; (dashed line) $[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}; (dashed-dotted line) $[\mathbf{12}]_0 = 3.0 \times 10^{-3}$ mol L^{-1}.

10^{-3} mol L^{-1}) and, therefore, $M_{n,th}$ ranging from 20,000 to 330,000 g mol^{-1} were studied (Fig. 7). It appears that the living fraction for the whole range of alkoxyamine concentration studied is between 90 and 50% at 50% of monomer conversion thus suggesting the preparation of high molar mass polystyrenes with good chain-end livingness. Moreover, the experimental molar masses obtained in this work are rather high compared to those generally targeted in the literature. These results at 60 °C are comparable to those obtained at 90 °C with SG1 nitroxide **1**.[25]

The influence of temperature on monomer conversion and living fraction was also investigated for temperatures ranging from 40 to 80 °C (Fig. 8 and Figure S5 in the Supporting Information). As expected, the temperature has a strong influence on the outcome of the polymerization. Indeed, whereas 600 h are needed to reach 50% conversion at 40 °C, only 60 h are necessary at 60 °C and 8 h at 80 °C. This slowing down of the kinetics with decreasing temperature is related to a lower concentration of macroradicals in the medium and thus led to a better livingness and a lower $Đ$ at high conversion. Conversely, an increase in temperature accelerates the kinetics, does not change significantly the control of the polymerization but is detrimental to the livingness of the resulting polymer. Indeed, as previously described,[26] an increase in temperature results in a decrease in livingness (e.g., at 50% conversion, 90 and 45% of living chains are obtained at 40 and 80 °C, respectively). Thus, a good compromise between the rate and the livingness of the polymerization process was obtained at 60 °C for the bulk polymerization of styrene mediated by alkoxyamine **12**.

EXPERIMENTAL

Materials

Benzene (Aldrich, 99%), ethylbenzene (Aldrich, 99%), and styrene (Aldrich, 99%) were distilled twice from calcium hydride and stored under argon. *N-tert*-butyl-*α-tert*-butyl nitrone **8** was synthesized as described previously.[33] All other materials were used as received.

Characterization

^{1}H NMR (200 MHz) measurements were performed on a Bruker AC 200 spectrometer at room temperature. ^{1}H NMR of hydroxylamine **9** was carried out in a 1:1 D_2O/C_3D_6O mixture after *in situ* reduction of nitroxide **10** by sodium dithionite. ESR spectra were recorded on a Bruker ESP-300 X-band spectrometer equipped with a HP 53150A frequency meter and a Boonton microwatt meter. Nitroxide concentrations were determined by integration of the ESR spectra and calibration with a known TEMPO solution in benzene. Size exclusion chromatography (SEC) was carried out at room temperature on a Shimadzu apparatus equipped with a refractometer (Shimadzu) and five columns PL GEL (10 μm particles) (three mixted B, 10^3 Å, 10^5 Å), using THF as eluent (flow rate: 1 mL min^{-1}). Calibration curves obtained from

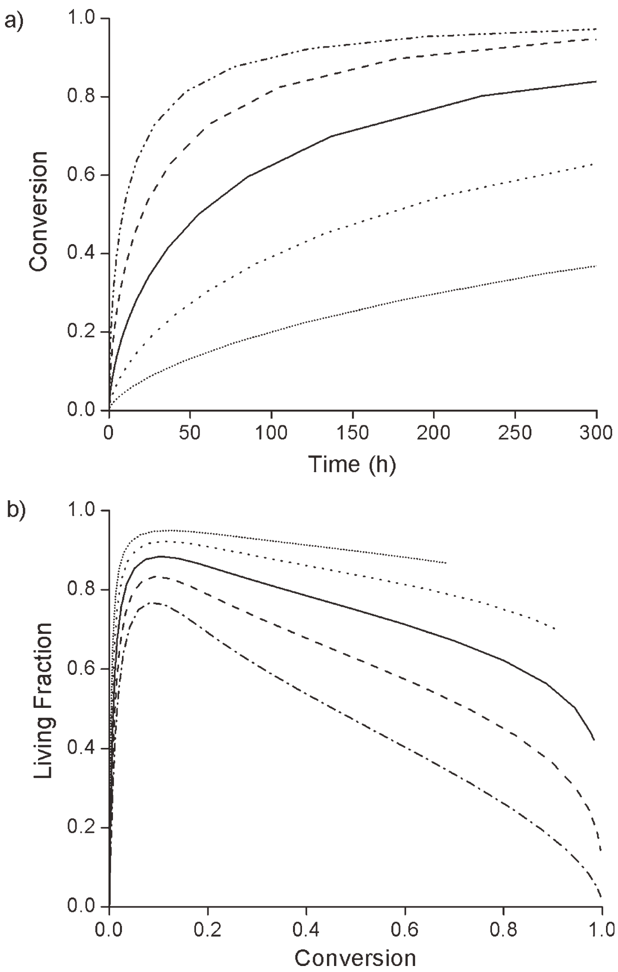


FIGURE 8 PREDICI modeling of the influence of the polymerization temperature on the bulk polymerization of styrene in the presence of alkoxyamine **12** ($[\mathbf{12}]_0 = 14.2 \times 10^{-3}$ mol L^{-1}): (a) conversion versus time; (b) living fraction versus conversion; (short dotted lines) 40 °C; (dotted lines) 50 °C; (solid lines) 60 °C; (dashed lines) 70 °C; (dashed-dotted lines) 80 °C.

polystyrene standards were used to calculate the number average molar masses (M_n) and dispersities (*Đ*).

Preparation of *sec*-Pentyllithium 7

A dispersion of 2-chloropentane (12 mL, 98 mmol) and lithium pieces (2.97 g, 429 mmol) in anhydrous benzene (100 mL) was stirred vigorously under argon during 72 h. After filtration under argon, the crude *sec*-pentyllithium **7** solution was titrated from acetanilide ([**7**] = 0.56 M).

Synthesis of *N-tert*-Butyl-*N*-(1-*tert*-butyl-2-methyl)pentyl Hydroxylamine 9

A solution of *sec*-pentyllithium, **7** (0.56 M, 27 mL, 15 mmol) in benzene was added dropwise, to a solution of *N-tert*-butyl-α-*tert*-butyl nitrone **8** (1.6 g, 10 mmol) in neat benzene (45 mL) at room temperature and under an argon atmosphere. The mixture was allowed to stir at room temperature during 6 h and was then quenched with a saturated solution of ammonium chloride (15 mL). The aqueous phase was extracted twice with methylene chloride (2 × 45 mL). The organic phase was then dried over $MgSO_4$, filtered, and evaporated under vacuum to give the crude hydroxylamine **9** (1.6 g, 70%) as a white solid.

^1H NMR (200 MHz, D_2O/C_3D_6O, δ, ppm): 0.91 (m, $(CH_3)_3CCH$, $CH_3CH_2CH_2$, 12H), 1.11 (s, $(CH_3)_3CN$, 9H), 1.16–1.47 (m, CH_3CH, $CH_3CH_2CH_2$, 7H), 1.82 (m, CH_3CH, 1H), 2.38 (m, $(CH_3)_3CCH$, 1H).

Synthesis of *N-tert*-Butyl-*N*-(1-*tert*-butyl-2-methyl)pentyl Nitroxide 10

A solution of the crude hydroxylamine **9** (0.5 g, 2.2 mmol) and $Cu(OAc)_2.H_2O$ (20 mg, 0.1 mmol) in methanol (15 mL) was stirred for 2 h under air bubbling. Methanol was then removed under vacuum and the crude mixture was purified by column chromatography eluting with cyclohexane to give nitroxide **10** (470 mg, 95%) as a red liquid. ESR (benzene): triplet, $a_N = 13.6$ G, $g = 2.0061$. Anal. calcd for $C_{14}H_{30}NO$: C, 73.62; H, 13.24; N, 6.13. Found: C, 73.81; H, 13.36; N, 6.08.

Synthesis of 1-Phenyl-1-(*N-tert*-butyl-*N*-(1-*tert*-butyl-2-methyl)pentyl nitroxide) Ethane 12

A degassed solution of nitroxide **10** (1.1 g, 5.0 mmol) and di-*tert*-butyl peroxalate (1.2 g, 5.1 mmol) [*Caution! Highly energetic compound and explosive when crystals are scratched!*] in ethylbenzene (15 mL, 123 mmol) was stirred at 35 °C under an argon atmosphere during 4 h. Excess ethylbenzene was then removed under vacuum at room temperature and the residue was purified by column chromatography eluting with cyclohexane. After evaporation of the solvent, pure alkoxyamine **12** (890 mg, 52%) was recovered as a pale yellow oil.

^1H NMR (200 MHz, $CDCl_3$, δ, ppm): δ 1.07 (s, $(CH_3)_3CCH$, 9H), 1.20 (2s, $(CH_3)_3CN$, 9H), 0.45–1.38 (m, $CH_3CH_2CH_2(CH_3)CH$, 10H), 1.47–1.64 (m, CH_3CHO, 3H), 2.41 (m, $CH_3CH_2CH_2(CH_3)CH$, 1H), 2.68–2.75 (2s, $(CH_3)_3CCH$, 1H), 5.00 (dq, CH_3CHO, 1H), 7.13–7.46 (m, aromatics, 5H). Anal. calcd for $C_{22}H_{39}NO$: C, 79.22; H, 11.78; N, 4.24. Found: C, 79.07; H, 11.97; N, 4.14.

Determination of the Rate Constant of Dissociation (k_d) by ESR Spectroscopy

A solution of alkoxyamine **12** (0.2×10^{-3} mol L^{-1}) and galvinoxyl (1×10^{-3} mol L^{-1}) in benzene was degassed by freeze-pump-thaw cycles, placed under argon and heated at temperatures between 60 and 100 °C. The release of the persistent radical during alkoxyamine dissociation was monitored by ESR spectroscopy. Nitroxide concentrations were determined by integration of the first peak of nitroxide **10** and calibration with a known 2,2,6,6-Tetramethylpiperidine 1-oxyl (TEMPO) solution in benzene.

Typical Polymerization Experiment

A solution of alkoxyamine **12** (50 mg, 0.15 mmol) in neat styrene (19.3 g, 185 mmol) was distributed among several glass tubes. The contents were degassed by freeze-pump-thaw cycles and the tubes were sealed off under vacuum. One tube was heated at 60 °C during 99 h, cooled down, and the polymerization medium was dissolved in THF. After evaporation of excess monomer and solvent, the polymer was freeze-dried in benzene. Conversion was evaluated gravimetrically, number average molar mass and dispersity were determined by SEC (yield = 61%, $M_n = 68{,}200$ g mol^{-1}, $Đ = 1.14$).

PREDICI Simulations

Modelings have been carried out with PREDICI (CIT), version 6.34 on a 2.53 GHz Intel Core i3 Macintosh computer using the CrossOver software. For all simulations, a PREDICI model comprising all the reaction steps and respective rate constants has been used. All the data are available in the Supporting Information section.

CONCLUSIONS

The peculiar structural and kinetic parameters of conveniently prepared nitroxide **10** and alkoxyamine **12** afforded an excellent control of the polymerization of styrene at 60 °C. The unprecendented observation of a true persistent radical effect for styrene with a rate of polymerization one order of magnitude higher than thermal polymerization was highlighted and accurately modeled using PREDICI. The results highlighted herein make nitroxide **10** a particularly promising candidate to investigate the control of other monomers already controlled by NMP (e.g., acrylates, acrylamides, isoprene) but also more challenging ones such as less activated monomers (e.g., vinyl esters, *N*-vinyl carbazole, …) as well as the formation of more sophisticated macromolecular architectures. Such studies are currently under investigation.

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