Ability of nitrones of various structures to control the radical polymerization of styrene mediated by in situ formed nitroxides

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Abstract

The ability of several nitrones to control the radical polymerization of styrene at 110 °C has been investigated by high-throughput experimentation. The nitrone/free radical initiator pair dictates the structure of the nitroxide and the alkoxyamine formed in situ, which determines the position of the equilibrium between the active and the dormant species operating in the nitroxide-mediated polymerization. For the styrene polymerization to be controlled, the nitrone must be reacted with 2,2′-azo-bis-isobutyronitrile (AIBN) at 85 °C, prior to addition of styrene and polymerization at 110 °C. The effect of the nitrone structure on the kinetics of the styrene polymerization has been emphasized. Amongst all the nitrones tested, those of the *C*-phenyl-*N*-*tert*-butylnitrone (PBN) type are the most efficient in terms of polymerization rate, control of molecular weight and polydispersity. Electrophilic substitution of the phenyl group of PBN by either an electrodonor or an electroacceptor group has only a minor effect on the polymerization kinetics. Importantly, the polymerization rate is not governed by the thermal polymerization of styrene but by the alkoxyamine formed in situ during the pre-reaction step. The initiation efficiency is, however, very low, consistent with a limited conversion of the nitrone into nitroxide and alkoxyamine.

Keywords: Nitroxide-mediated polymerization; Nitrone; Polymerization kinetics

1. Introduction

Nowadays, a tremendous research activity is devoted to advanced polymeric materials with controlled macromolecular structures and new and/or improved macroscopic properties. Controlled radical polymerization (CRP) has expanded very rapidly in the recent years [1-4], and contributes effectively to the macromolecular engineering of synthetic polymers. The nitroxide-mediated polymerization (NMP) is a very efficient CRP system, based on the pioneering works by Rizzardo [5] and [6], and Georges [7-9], who used 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the mediating radical.

The NMP mechanism is based on the reversible capture of the propagating species by nitroxides with formation of thermally labile alkoxyamines (dormant chains). At high temperature, the dormant species release polymeric radicals able to add some monomer units before recombination with nitroxides. Whenever this equilibrium between active and dormant species is shifted towards the dormant species, the instantaneous concentration of radicals (propagating species) is decreased and the extent of the irreversible termination reactions is limited. Moreover, a rapid exchange between active and dormant species is required for all the chains to propagate at the same rate.

Because only the polymerization of styrene and derivatives was controlled by TEMPO at high temperature and for long reaction times, the structure of the nitroxide was modified and the controlled polymerization was extended to other monomers. For instance, functional TEMPO, such as 4-*oxo*-TEMPO, was used in the polymerization of styrene and acrylates [10]. Later on, more active acyclic nitroxides containing an α-hydrogen, such as DEPN (*N*-*tert*-butyl-*N*-(1-di-ethylphosphono-2,2-dimethylpropyl)-*N*-oxyl) [11-17] and TIPNO (2,2,5,5-tetramethyl-4-phenyl-3-azahexane-3-oxyl) [18] and [19], were developed with great success in the controlled radical polymerization of a broader range of monomers, including styrene and derivatives, acrylates, acrylamide, acrylonitrile, acrylic acid and dienes. Recently, an alkoxyamine derived from TIPNO was prepared in one-step [20] and used in the controlled radical polymerization of styrene and isoprene at 125 °C. The radical polymerization of acrylates did not fall under control with this alkoxyamine. The structure of the nitroxide is thus one of the key features for the success or failure of NMP [21]. Moreover, Catala et al. recently developed

new acyclic α-hydrogen containing nitroxides with a sulfoxide group in β-position (*N-tert*-butyl-(1-*tert*-butyl-2-ethylsulfinyl)propyl nitroxide or BESN) and the parent alkoxyamines [22-23]. Control was imparted to the radical polymerization of styrene, ethyl and *n*-butylacrylate at quite low temperatures (100 and 90 °C, or below), which emphasizes again that the structure of the nitroxide has a decisive effect on the position of the equilibrium between the active and the dormant species [21], and thus on the control of the NMP process.

More recently, several research groups focused on the direct formation of nitroxide and alkoxyamines in the polymerization medium from appropriate precursors. This in situ NMP concept was first tested with nitrones and nitroso compounds as precursors [24-26]. These two compounds are well known spin-trapping agents [27-34] that react with radicals with formation of nitroxide (Scheme 1). Later on, Grishin et al. reported on the controlled radical polymerization of methylmethacrylate (MMA) [34-36], *n*-butylmethacrylate (BMA), *n*-butylacrylate (*n*BuA)[37-38], styrene (S) [39], and styrene/acrylonitrile (SAN) [40] initiated by traditional free radical initiators in the presence of *C*-phenyl-*N-tert*-butylnitrone (PBN) or *N*,α-diphenylnitrone (DPN). Molecular weight distribution was, however, broad ($1.3 \leq M_w/M_n \leq 3.65$), and synthesis of block copolymers was not reported. Golubev et al. used *C*-phenyl-*N-tert*-butylnitrone (PBN) in order to mediate the radical polymerization of styrene initiated by benzoyl peroxide (BPO) in a temperature range from 90 to 120 °C [41]. At high temperature, the polymerization was pseudo-living, the polymerization of styrene could be resumed and PS-*b*-PnBuA was synthesized by sequential polymerization of styrene and *n*-butylacrylate with the intermediate recovery of the PS chains. The use of *N-tert*-butyl-α-isopropylnitrone (nitrone **1**, Scheme 2) together with BPO proved efficiency in controlled bulk polymerization of styrene at 110 °C [42]. Well-defined styrene containing random and block copolymers (PSAN, PS-*b*-PSAN, PS-*b*-PnBuA and PS-*b*-PIP) with a low polydispersity were accordingly synthesized (where PIP stands for polyisoprene).
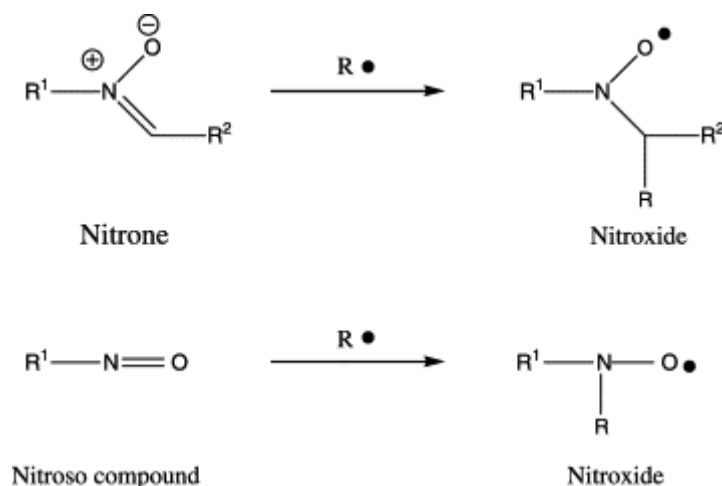
Scheme 1.
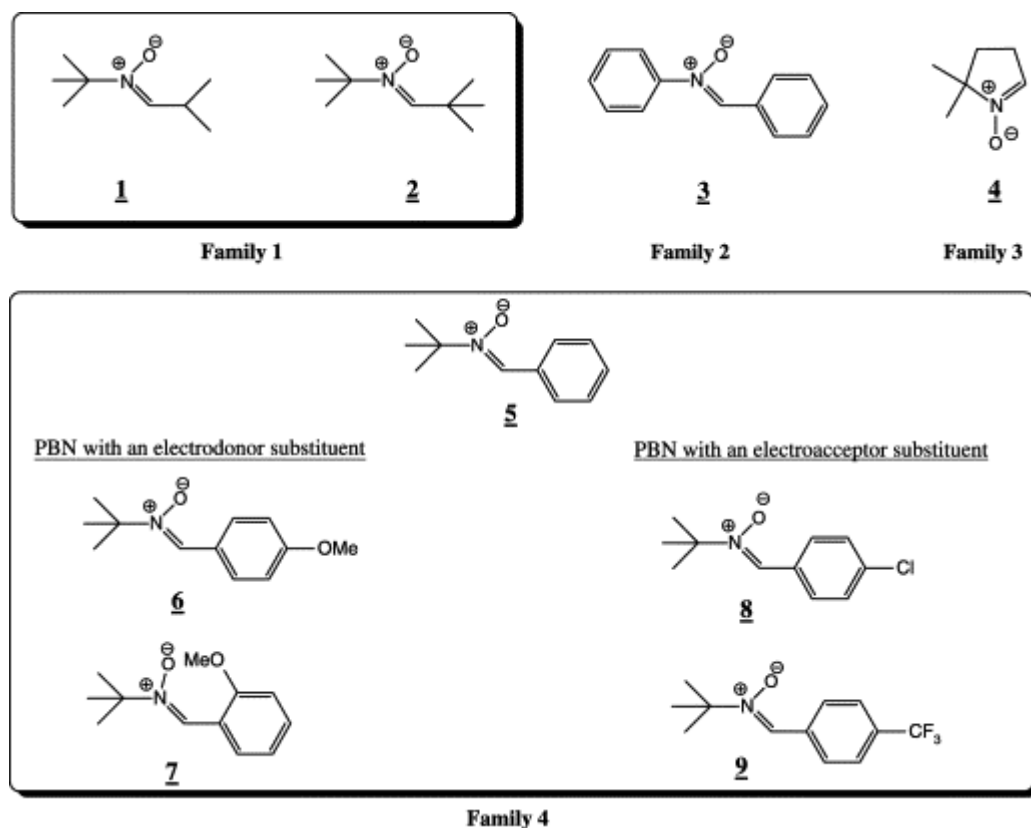
Scheme 2. Library of nitrones (precursors of nitroxides) tested in the control of the free radical polymerization of styrene. N-tert-Butyl-α-isopropylnitrone 1, N-tert-butyl-α-tert-butylnitrone 2, N,α-diphenylnitrone 3 (DPN), 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) 4, C-phenyl-N-tert-butylnitrone (PBN) 5, C-(4-methoxyphenyl)-N-tert-butylnitrone (4-OMe-PBN) 6, C-(2-methoxyphenyl)-N-tert-butylnitrone (2-OMe-PBN) 7, C-(4-chlorophenyl)-N-tert-butylnitrone (4-Cl-PBN) 8, C-[4-(α,α,α-trifluoromethyl)phenyl]-N-tert-butylnitrone (4-CF₃-PBN) 9.

This paper aims at screening a series of nitrones as precursors of nitroxides and alkoxyamines in the in situ NMP of styrene. Part of this study is based on high-throughput experimentation which is steadily more extensively used in the polymer field [43-44]. Hawker et al. took advantage of this type of experimentation for testing a library of alkoxyamines in NMP [45]. The purpose of this work is to investigate the effect of the structure of the nitrones on the kinetics and control of a 'standard' radical polymerization, that one of styrene. As soon as the rules that govern the in situ NMP based on nitrones will be known, this type of process will be extended to more difficult systems, such as acrylates. In situ NMP has also been conducted in bulk and in solution for sake of comparison. The importance of the nitrone/initiator pair on the control of the polymerization will also be reported.

2. Experimental part

2.1. Materials

Styrene (Aldrich, 99+%) was dried over calcium hydride (CaH_2) and distilled before use in order to remove the stabilizer. Toluene (Aldrich) was degassed prior to use. AIBN (Aldrich, >98%) was used as received. *N-tert*-Butyl-α-isopropylnitrone **1** (Scheme 2) and *N-tert*-butyl-α-*tert*-butylnitrone **2** (Scheme 2) were synthesized as reported elsewhere [18]. PBN type nitrones (Scheme 2) were synthesized according to Janzen et al. [46]. The *N,α*-diphenylnitrone **3** (DPN) (Lancaster, 97%) and the cyclic nitrone 5,5-dimethyl-1-pyrolidin-*N*-oxide **4** (DMPO) (Aldrich, 97%) were used as received (Scheme 2). All the synthesized nitrones were characterized by ^{1}H NMR, IR, elemental analysis and melting point. The experimental data were in good agreement with the published data [18] and [46].

2.2. Instrumentation

In the high-throughput experimentation, pre-reactions and polymerizations were carried out with a Chemspeed ASW 2000 automated synthesizer and 15 ml reactors blocks (equipped with a heating/cooling jacket and cold-finger reflux condensers) [47]. Addition of compounds and sampling of the polymerization medium were performed with the fully automated liquid handling system of the synthesizer. The reaction medium was stirred by the vortex system of the equipment.

2.3. General recipe for the radical polymerization of styrene using the nitrone/AIBN system in the automated synthesizer (styrene/nitrone: 45/1 and nitrone/AIBN: 1/0.5)

All liquids were transferred under argon by glass syringes with stainless steel capillaries through rubber septa. Reactors of the automated synthesizer were first heated at 140 °C under reduced pressure for 15 min, and then filled with argon. This treatment was repeated three times prior to experimentation under argon. A 0.39 M solution of the desired nitrone and a 0.19 M solution of the radical initiator (AIBN) (both the compounds being previously degassed by three argon-vacuum cycles) were prepared in degassed toluene. One millilitre of each solution was added to the reactors of the automated synthesizer for the nitrone and the radical initiator to be pre-reacted. Temperature of the reactors and condensers was 85 and 5 °C, respectively. After 4 h of pre-reaction under 600 rpm stirring, temperature of the reactors was decreased to 50 °C, the vortex was stopped and degassed styrene (2 ml, 1.75×10^{-2} mol) was added. The vortex was started again and temperature of the reactors was increased to 110 °C. Monomer conversion was monitored by sampling 400 µl of the reaction mixture with the automated liquid handling system at pre-determined times. Residual monomer and toluene were removed under vacuum at 80 °C, the residue was weighed and the monomer conversion was calculated by taking the original amounts of nitrone and AIBN into account.

2.4. General recipe for the bulk polymerization of styrene using the nitrone/AIBN system (styrene/nitrone: 45/1 and nitrone/initiator: 1/0.5)

A mixture of the desired nitrone (3.9×10^{-4} mol) and the conventional radical initiator AIBN (0.0318 g, 1.9×10^{-4} mol) was degassed by three argon-vacuum cycles. Degassed toluene (2 ml) was added and the reaction medium was heated at 85 °C for 4 h. After this pre-reaction, toluene was removed under vacuum at room temperature, degassed styrene (2 ml, 1.75×10^{-2} mol) was added and the flask was heated at 110 °C under argon. Samples were picked out regularly from the polymerization medium with a glass syringe and a stainless steel capillary. Monomer conversion was calculated by gravimetry as aforementioned.

2.5. Characterization

^{1}H NMR spectra were recorded in CDCl$_3$ with Bruker AM 250 and 400 MHz spectrometers at room temperature. IR spectra of nitrones were recorded with a Perkin–Elmer spectrometer, the nitrones being solvent (THF) cast on sodium chloride plates. Size exclusion chromatography (SEC) was carried out in THF at 45 °C with a HS chromatograph equipped with a Cfloam isotactic pump 301, a SFD autosampler S 5200 P and a SFD refractive index detector 2000 (columns PL gel 5 µm (10^5, 10^4, 10^3, 100 Å)) and calibrated with polystyrene standards. The flow rate was 1 ml/min.

3. Results and discussion

3.1. Styrene polymerization in the presence of different types of nitrones: conditions of control and polymerization kinetics

A previous work reported that control could be imparted to the radical polymerization of styrene provided that a nitrone, e.g. *N-tert*-butyl-α-isopropylnitrone **1** (Scheme 2), was pre-reacted with styrene and BPO at 85 °C, followed by polymerization at 110 °C [42]. During this pre-reaction, nitroxides are formed with a hardly predictable structure, because the nitrone can react with different radicals, i.e. the PhCOO and Ph. radicals released by BPO, and the propagating polystyryl radicals (Scheme 3). Substitution of AIBN, that produces only one type of radicals, for BPO is a way to decrease the complexity of the system, as illustrated in Scheme 3. Unfortunately, the styrene polymerization is out of control when AIBN is used. No improvement is observed when the pre-reaction with AIBN is conducted at 76 °C, thus when the half-life time of AIBN is comparable to that one of BPO at 85 °C [42]. In another approach, the nitrone **1** was pre-reacted with AIBN in the absence of

styrene at 85 °C in toluene, in order to form the parent nitroxide and alkoxyamine. After 4 h of pre-reaction, toluene is removed under vacuum, styrene is added and polymerized at 110 °C. Although the number-average molecular weight increases linearly with the monomer conversion (Fig. 1), the straight line does not pass through the origin, which suggests a fast propagation compared to the establishment of the equilibrium between active and dormant species. A reason might be either the slow cleavage of the in situ formed alkoxyamine and/or the slow recombination of the parent nitroxide with propagating chains, consistent with formation of polystyrene with high M_n (~19,500 g/mol) and polydispersity (M_w/M_n: 1.7–2 or higher) in the early stage of polymerization. Furthermore, the time dependence of $\ln([M]_0/[M])$ (Fig. 2) is linear, and polydispersity is high (M_w/M_n: 1.7–2 or higher) in line with the occurrence of side reactions. Control of the radical polymerization of styrene by this *N*-*tert*-butyl-α-isopropylnitrone **1**/AIBN system at 110 °C is thus poor, in sharp contrast to the effective control observed when BPO is used rather than AIBN [42]. Clearly, the structure of both the nitrone and the radicals formed in the polymerization medium dictates the structure of the in situ formed nitroxide (Scheme 1 and Scheme 3) and has a decisive effect on the issue of the NMP process.
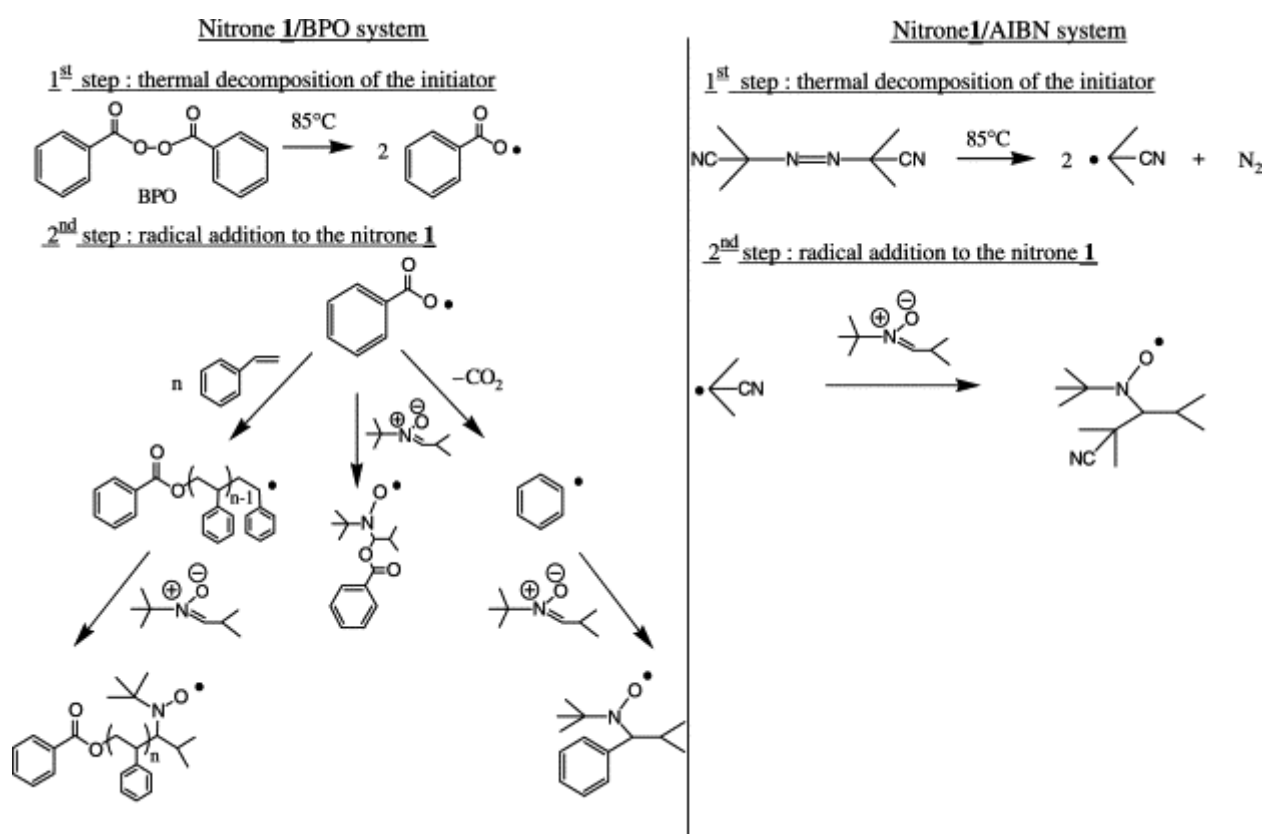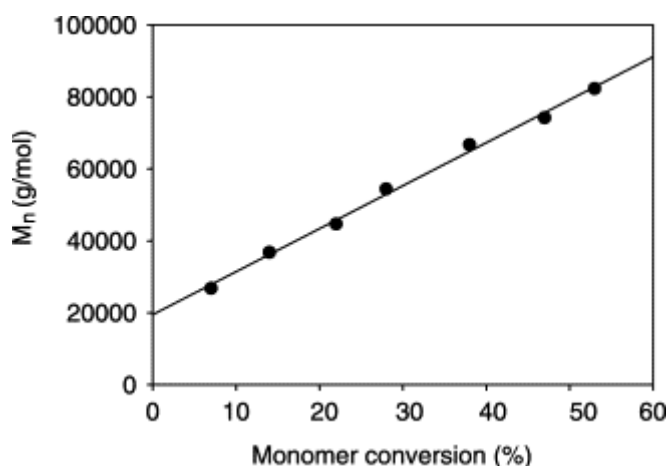

Scheme 3.

*Fig. 1. Dependence of $M_{n,SEC}$ on the styrene conversion for the bulk radical polymerization of styrene at 110 °C [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone **1**]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone **1**: 90/1].*
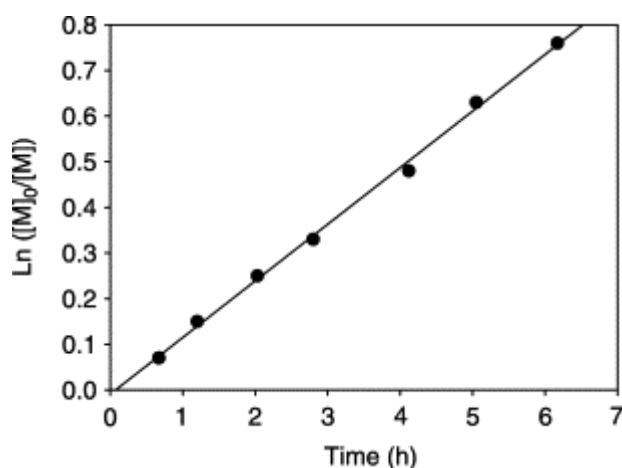

*Fig. 2. Time dependence of ln ([M]$_0$/[M]) for the bulk radical polymerization of styrene at 110 °C [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone **1**]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone **1**/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone **1**: 90/1].*

In the next series of experiments, several nitrones have been used in order to change the structure of the in situ formed nitroxides and, thus, the course of the polymerization. For sake of comparison, the same free radical initiator, AIBN, has been used in all the experiments. The nitrones under consideration, have been classified in four families, as reported in Scheme 2. The ability of all these nitrones to control the radical polymerization of styrene has been investigated by high-throughput experimentation with a 15 ml automated parallel synthesizer. The viscosity of the polymerization medium has been decreased by addition of toluene (styrene/toluene: 1/1, v/v) for samples to be easily picked out through the needle of the automated synthesizer. Dependence of molecular weight on the monomer conversion and time dependence of ln([M]$_0$/[M]) are illustrated for each family of nitrones in Fig. 3 and Fig. 4. The effect of the nitrones **1** and **2** on the styrene polymerization has been compared in relation to the substitution of a *tert*-butyl group (nitrone **2**) for the isopropyl group of the nitrone **1**. The higher molecular weights observed with the nitrone **2**/AIBN system, indicate a decrease in the initiation efficiency ($f=M_{n,theor.}/M_{n,exp.}$) (Fig. 3 and Table 1). The theoretical molecular weights, $M_{n,theor.}$, have been calculated on the basis of the initial amount of nitrone that was previously shown to control the molecular weight of polystyrene [42]. Amplified steric effect of the *tert*-butyl group compared to the isopropyl one is more likely at the origin of this loss of initiation efficiency. The addition of cyanoisopropyl radicals to the nitrone **2** would indeed be more sterically hindered, resulting in a lower amount of nitroxide and/or alkoxyamines, and thus in polystyrene chains of a higher molecular weight. Moreover, the concentration of the in situ formed nitroxides would be low compared to AIBN left undecomposed (~2% of the initial amount [48]) at the end of the pre-reaction at 85 °C.

This situation can account for the fast monomer consumption at the early stage of polymerization (burst effect), followed by a decrease in the propagation rate which ultimately falls under control of the thermal polymerization of styrene at 110 °C (Fig. 4). Polydispersity indices are rather high (M_w/M_n: 1.6–2), although slightly lower with the nitrone **2** (1.6–1.7) (Fig. 5). Substitution of a phenyl group (N,α-diphenylnitrone or DPN, nitrone **3**) for the alkyl group of the nitrones **1** and **2** does not improve the situation, particularly with respect to the polydispersity of polystyrene (Fig. 5). In contrast to the dependence of the number-average molecular weight on the monomer conversion which is linear (Fig. 3), the time dependence of $\ln([M]_0/[M])$ shows an upward curvature (Fig. 4), which might be due to the slow decomposition of nitroxide during the polymerization process.
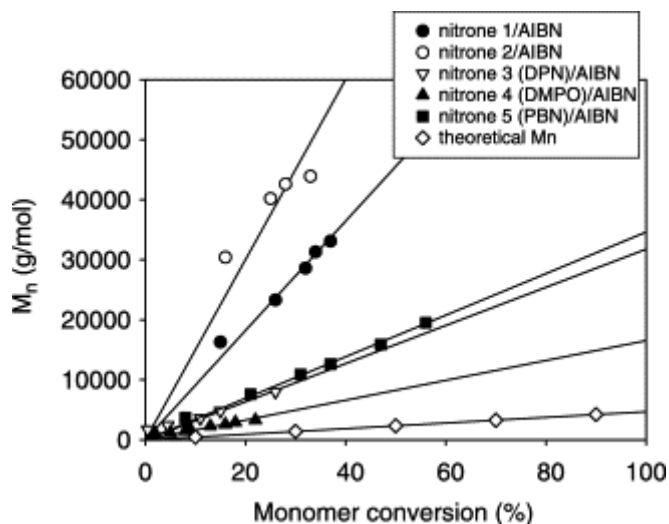
*Fig. 3. Dependence of $M_{n,SEC}$ on the styrene conversion for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v), in the presence of various nitrones (**1→5**, Scheme 3) [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1].*
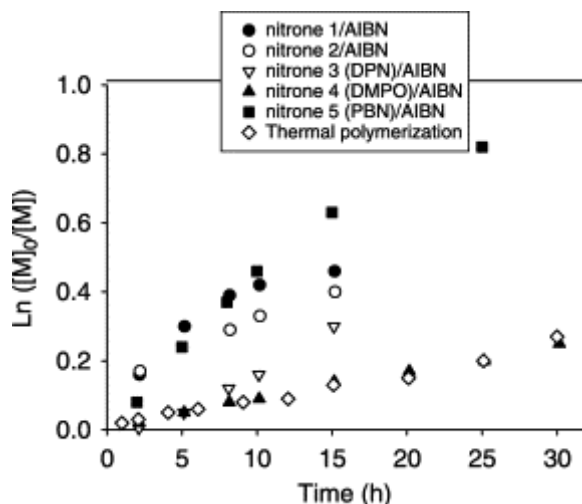

*Fig. 4. Time dependence of $\ln([M]_0/[M])$ for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v), in the presence of various nitrones (**1→5**, Scheme 3) [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1].*

Table 1. Radical polymerization of styrene in toluene at 110 °C in the presence of various nitrones together with AIBN

Nitrone	Time (h)	Conv. (%)	$M_{n,SEC}$ (g/mol)	$M_{n,theor.}$ (g/mol)	f ($M_{n,theor.}/M_{n,exp.}$)
1	2.18	15	16,500	700	0.04
	5.18	26	23,500	1200	0.05
	8.18	32	28,500	1500	0.05
	10.18	34	31,500	1600	0.05
	15.18	37	33,000	1700	0.05
2	2.2	16	30,500	750	0.02
	8.2	25	36,000	1200	0.03
	10.2	28	40,000	1300	0.03
	15.2	33	42,500	1500	0.04
	20.2	36	44,000	1700	0.04
3	8.13	11	3500	500	0.14
	10.13	15	5000	700	0.15
	15.13	26	8000	1200	0.15
4	8.15	8	1500	380	0.25
	15.15	13	2500	610	0.26
	25.15	18	3000	850	0.29
	30.15	22	3500	1030	0.31
5	2	8	3500	380	0.10
	5	21	7500	980	0.13
	8	31	11,000	1450	0.13
	10	37	12,500	1730	0.14
	15	47	16,000	2200	0.14
	25	56	19,500	2620	0.13

Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.39 M and [AIBN]=0.19 M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1 and styrene/toluene: 1/1, v/v.
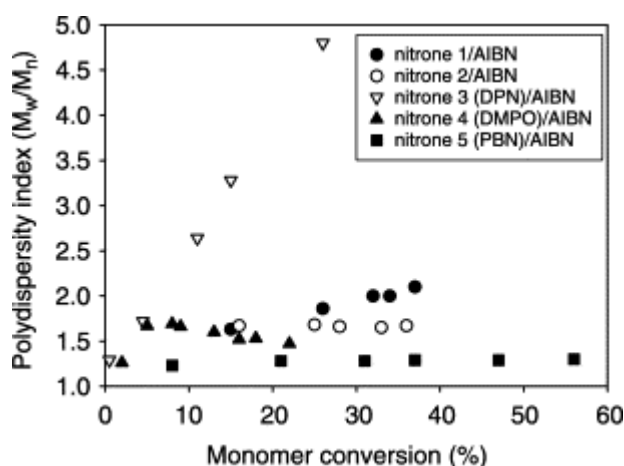
*Fig. 5. Dependence of the polydispersity index (M_w/M_n) on the styrene conversion for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v), in the presence of various nitrones (**1→5**, Scheme 3)*

[Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1].

In the presence of a cyclic nitrone (5,5-dimethyl-1-pyrolidin-*N*-oxide or DMPO, nitrone **4**), a linear dependence is observed for both the number-average molecular weight on the monomer conversion and the monomer consumption on time (Fig. 3 and Fig. 4). The propagation rate is typically governed by the thermal polymerization of styrene (same slope for the time dependence of $\ln([M]_0/[M])$). The polydipersity is rapidly high ($M_w/M_n \approx 1.7$) and then decreases with increasing monomer conversion (Fig. 5). Importantly, the initiation efficiency *f* (Table 1) is significantly improved, consistent with a larger amount of nitroxide formed in the medium compared to the previously tested nitrones **1** and **2**. The small induction period observed with the nitrones **3** and **4**, more likely results from the higher amount of nitroxide formed in the medium by these nitrones. During this induction period, part of the nitroxide formed during the pre-reaction, is rapidly trapped by styryl radicals formed by autopolymerization of styrene at 110 °C or by radicals released by AIBN left unreacted at the end of the pre-reaction. When the excess of nitroxide is consumed, the polymerization proceeds according to a NMP process.

Finally, *C*-phenyl-*N*-*tert*-butylnitrone **5** (PBN) has been tested. The number-average molecular weight of polystyrene increases linearly with the monomer conversion (Fig. 3) and so does $\ln([M]_0/[M])$ with time, although not beyond 40% conversion (Fig. 4). Moreover, the polydipersity is rather low and essentially independent of the monomer conversion ($M_w/M_n \approx 1.3$) (Fig. 5). The loss in the linearity of $\ln([M]_0/[M])$ versus time (curvature in Fig. 4) indicates that the concentration of the propagating species, and thus the propagation rate, are decreasing with time. Nevertheless, the polymerization rate (R_p) remains much higher than the thermal polymerization rate (R_{th}) for the first 10 h (R_p/R_{th}=5.32) (the same behavior was observed for nitrones **1** and **2**). This characteristic feature is also observed for the bulk polymerization (Fig. 6). In that case, toluene is removed after the pre-reaction, followed by addition of styrene at room temperature and polymerization at 110 °C. The time dependence of $\ln([M]_0/[M])$ is linear until quite high monomer conversion (~70%) (Fig. 6), in agreement with a constant concentration of the propagating species. The bulk polymerization rate is 2.34 times higher than the thermal polymerization rate under the same conditions. In these experiments, the polymerization rate (R_p) is not governed by the initiating radicals produced by the auto-initiation of styrene and thermolysis of AIBN but rather by thermolysis of the alkoxyamine of the dormant chains. Fischer [49-50] and Fukuda et al. [51] and [52] have established power laws, that predict the time dependence of both the monomer consumption and the concentration of persistent radicals (nitroxides) (Eqs. Figs. (1a) and (1b)) whenever the polymerization is selectively initiated by an alkoxyamine. However, whenever thermal initiation (auto-initiation of styrene) is not negligible or in the presence of a radical initiator, Eqs. Figs. (2a) and (2b) are valid, and the system reaches a stationary state.

$$\ln\left(\frac{[M]_0}{[M]}\right) = \left(\frac{3k_p}{2}\right)\left(\frac{K[P-X]_0}{3k_t}\right)^{1/3} t^{2/3} \tag{1a}$$

$$[X^.] = (3k_t K^2 [P-X]_0^2)^{1/3} t^{1/3} \quad \text{(concentration of nitroxide)} \tag{1b}$$

$$\ln\left(\frac{[M]_0}{[M]}\right) = k_p \left(\frac{Ri}{k_t}\right)^{1/2} t \quad \text{(stationary state)} \tag{2a}$$

with $(Ri/k_t)^{1/2} = [P^.]$ (concentration of transient radicals)

$$[X^.] = \frac{K[P-X]}{[P^.]}, \quad K = \frac{k_d}{k_c} \quad \text{(stationary state)} \tag{2b}$$

where k_p is the propagation rate constant; k_t is the irreversible termination rate constant; R_i is the initiation rate, K is the equilibrium constant; k_d is the dissociation rate constant; k_c is the combination rate constant and $[P-X]_0$ is the initial concentration of the dormant species.
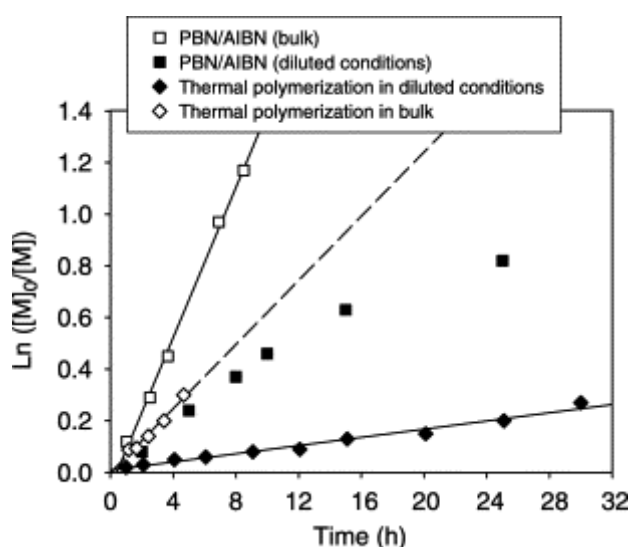

Fig. 6. Time dependence of ln ([M]₀/[M]) for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v) and in bulk, in the presence of PBN [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10⁻² M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C with or without toluene; styrene/nitrone: 45/1].

It might be anticipated that the radical polymerization of styrene, in the presence of the PBN/AIBN system and after 4 h of pre-reaction at 85 °C, obeys Eqs. Figs. (1a) and (1b) because the polymerization rate is higher than the thermal polymerization rate, and thus depends on alkoxyamine concentration. However, $\ln([M]_0/[M])$ is directly proportional to time t (Fig. 6) and not to $t^{2/3}$. This discrepancy could be explained by the formation of an alkoxyamine together with an excess of nitroxide during the pre-reaction at 85 °C. An excess of nitroxide, when the polymerization starts at 110 °C, would impede or at least restrict importantly the persistent radical effect [49] and [50], that consumes alkoxyamines and releases nitroxides. In other words, the active species $P^.$ would react preferably with the nitroxide $X^.$ rather than being terminated irreversibly, which is the case whenever the alkoxyamine does not coexist with an excess of nitroxide. The small induction period (~30 min) which is observed when the polymerization of styrene is initiated at 110 °C (Fig. 6), is the time necessary to consume part of the nitroxide excess formed during the pre-reaction, and to reach the stationary state. The nitroxide concentration $[X^.]$ thus decreases at the early stage of polymerization, although it increases when the polymerization is selectively initiated by an alkoxyamine. Therefore, when the PBN system is concerned, the polymerization rate (Eq. (3)) is governed by the equilibrium constant, the nitroxide concentration at the stationary state $[X^.]_{stat}$ and the alkoxyamine concentration $[P-X]_0$ which remains constant during polymerization (when the bulk polymerization is concerned). After the induction period, the $[P-X]_0/[X^.]_{stat}$ ratio is thus constant during the whole polymerization.

$$\ln\left(\frac{[M]_0}{[M]}\right) = k_p K \left(\frac{[P-X]_0}{[X^.]_{stat}}\right) t \tag{3}$$

where $[X^{\bullet}]_{stat}=[X^{\bullet}]_0-[X^{\bullet}]_{consumed\ during\ the\ induction\ period}$. $[X^{\bullet}]_0$ is the nitroxide concentration at the end of the pre-reaction.

Fig. 7 shows that M_n increases linearly with the monomer conversion and that the initiation efficiency ($f=M_{n,theor.}/M_{n,exp.}$) is higher for bulk polymerization ($f=0.22$) than for polymerization in solution ($f=0.13$). Fig. 8 is another illustration of the control of the bulk polymerization of styrene. Indeed, the SEC chromatograms are systematically shifted as a whole to smaller elution volumes with increasing styrene conversion. A tailing on the low molecular weight side is, however, observed which more likely results from dead polymer chains formed in the early stage of polymerization, thus when the equilibrium between dormant and active species is establishing (persistent radical effect).
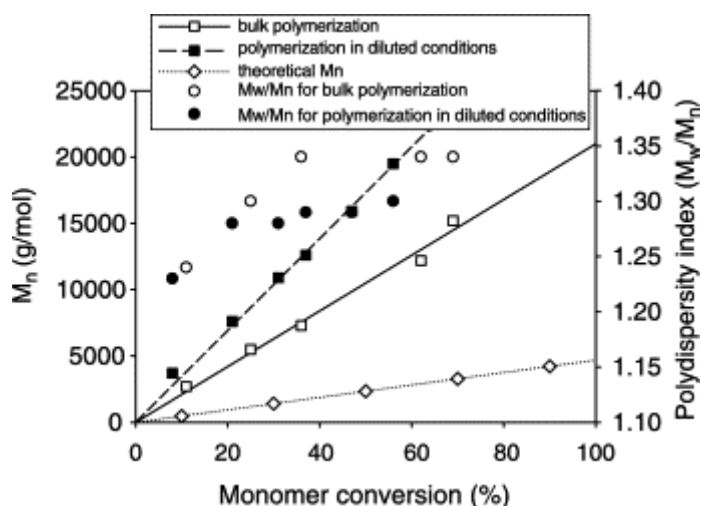

Fig. 7. Dependence of $M_{n,SEC}$ and polydispersity index on the styrene conversion for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v) and in bulk, in the presence of PBN [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C with or without toluene; styrene/nitrone: 45/1].
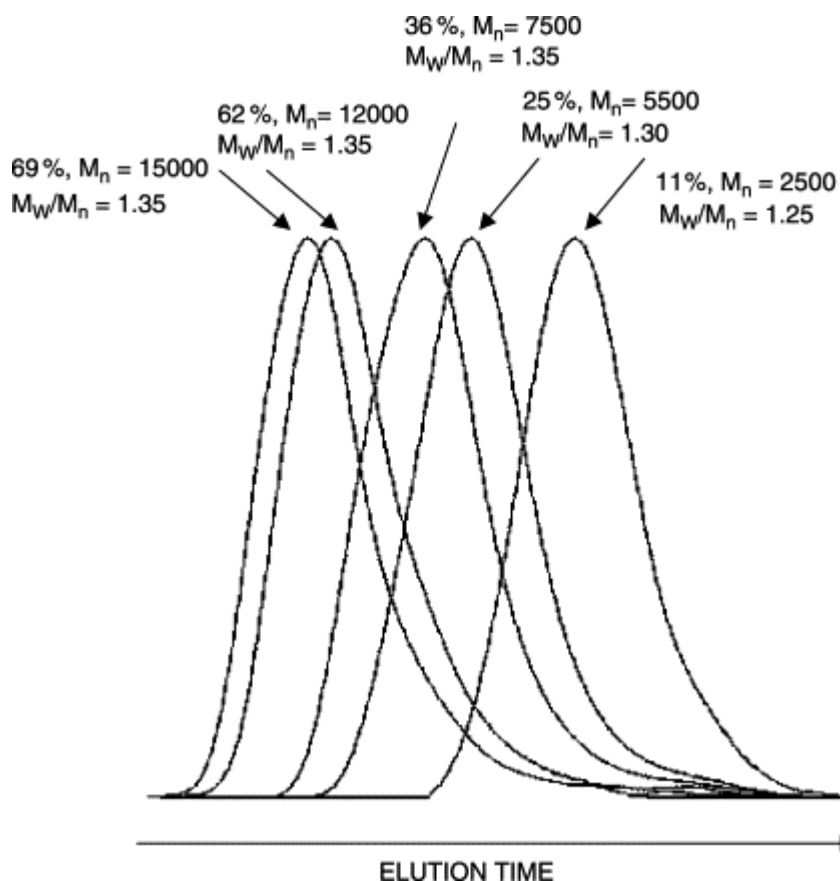
Fig. 8. SEC chromatograms for the bulk polymerization of styrene at 110 °C in the presence of PBN [Pre-reaction of PBN and AIBN in toluene at 85 °C for 4 h; [PBN]=0.19 M and [AIBN]=9.7×10⁻² M (PBN/AIBN: 1/0.5). Polymerization at 110 °C; styrene/PBN: 45/1].

The decrease in the polymerization rate, which is observed in solution at higher reaction times, results from irreversible termination reactions responsible for the increase of nitroxide concentration. This slow increase in the nitroxide concentration is thus decreasing the $[P{-}X]_0/[X^{\bullet}]_{stat}$ ratio and induces the curvature of $\ln([M]_0/[M])$ versus time plot (Eq. (3)).

A large discrepancy between the experimental and theoretical molecular weights (poor initiation efficiency *f*) is observed for all the nitrone systems tested (Table 1). This low initiation efficiency would indicate that only a small amount of the initial nitrone was converted into nitroxides and alkoxyamines. This factor was greatly improved in the presence of the cyclic nitrone **4** (DMPO) compared to the non-cyclic ones. This higher initiation efficiency would indicate that the yield of nitroxides starting from DMPO (nitrone **4**) and AIBN would be higher compared to the other nitrones.

3.2. Comparison of nitrones of the PBN family: Effect of substitution of the phenyl group

Because the PBN/AIBN system provides the radical polymerization of styrene with control, the efficiency of PBN derivatives has been tested. They have been prepared by substitution of the phenyl group in either *para* or *ortho* position with electrodonor and electroacceptor groups, respectively, (Scheme 2). This systematic comparison has been carried out in solution with the automated synthesizer (styrene/toluene: 1/1; v/v). The evolution of the number-average molecular weight with the monomer conversion is linear (Fig. 9), and the polydipersity indices are low ($1.2 \leq M_w/M_n \leq 1.35$). The time dependence of $\ln ([M]_0/[M])$ is also linear at least for 10 h followed, in some cases, by a decrease of the polymerization rate (Fig. 10). Moreover, the polymerization rate is systematically higher than the thermal polymerization consistent with a dependence on the alkoxyamine concentration. Thus, it is shown for the first time that the polymerisation rate in the in situ NMP process is not dominated by the kinetics of the thermal polymerisation, as is the case for NMP in the presence of TEMPO. As a rule, substitution of the phenyl group of PBN has only minor effect on the addition of the cyanoisopropyl radicals and the constant of the equilibrium between nitroxide and alkoxyamine. The major difference in the

experimental data is observed for PBN substituted by a methoxy group in *para* position of the phenyl group (4-OMe-PBN, nitrone **6** in Scheme 2). The number-average molecular weight is indeed higher (Fig. 9) and the molecular weight distribution is slightly broader.
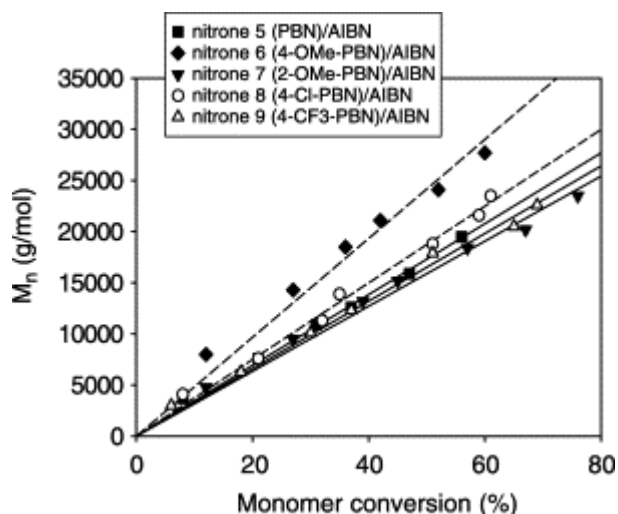

Fig. 9. Dependence of $M_{n,SEC}$ on the styrene conversion for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v), in the presence of PBN type of nitrones [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1].

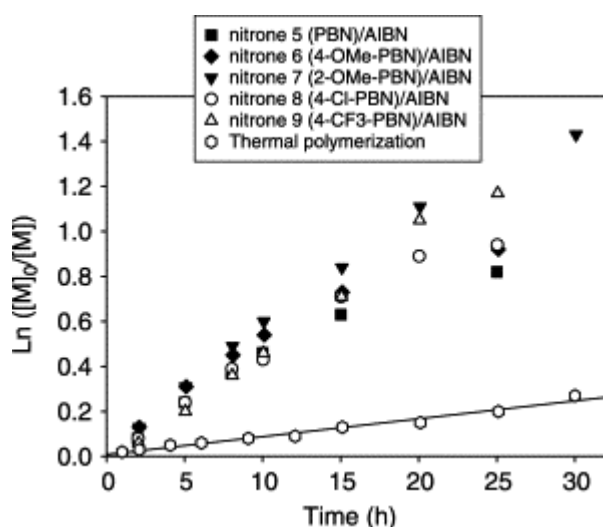*Fig. 10. Time dependence of ln ([M]$_0$/[M]) for the radical polymerization of styrene at 110 °C in toluene (styrene/toluene: 1/1; v/v), in the presence of PBN type of nitrones [Pre-reaction of nitrone and AIBN in toluene at 85 °C for 4 h; [nitrone]=0.19 M and [AIBN]=9.7×10^{-2} M (nitrone/AIBN: 1/0.5). Polymerization at 110 °C; styrene/nitrone: 45/1].*

4. Conclusions

A series of nitrones have been screened by high-throughput experimentation on the basis of their capacity to generate nitroxides and alkoxyamines in situ and to control the radical polymerization of styrene. The nitrone/free radical initiator pair dictates the structure and yield of the nitroxides and parent alkoxyamines formed in situ, and determines the position of the equilibrium between active and dormant species. Most of the tested nitrones have a beneficial effect on the control of the radical polymerization of styrene at 110 °C, the higher efficiency being the privilege of nitrones of the PBN type. It must be noted that the best control of the

styrene polymerization is observed when the nitrone is pre-reacted with the radical initiator (AIBN) at 85 °C, thus prior to addition of styrene and polymerization at 110 °C. The control persists until high monomer conversion, particularly for bulk polymerization, and the polymerization rate is high. When the phenyl group of PBN is substituted by an electrodonor (–OMe) or an electroacceptor (–Cl, –CF$_3$) group in *ortho* or *para* position, only minor changes are observed in the polymerization kinetics. In all the cases, the experimental molecular weights are much higher than the theoretical values, consistent with a very low initiation efficiency. Importantly, the styrene polymerization rate, R_p, in the presence of PBN type of nitrones is much higher than the styrene thermal polymerization rate, R_{th}, which emphasizes the decisive effect of the alkoxyamine concentration on the polymerization kinetics. This study shows good improvements in terms of rate of polymerization and polydispersity indices compared to previous works [39-41] in which nitrone and initiator are directly reacted in the presence of styrene.

In order to go a step further in the understanding of this NMP process based on the in situ formation of the nitroxides and alkoxyamines, an ESR investigation is highly desirable and will be carried out in the near future.

Acknowledgements

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