Design and Use of β-Phosphorus Nitroxides and Alkoxyamines in Controlled/"Living" Free Radical Polymerizations

*Christophe Le Mercier, Sébastien Acerbis, Denis Bertin, Florence Chauvin, Didier Gigmes, Olivier Guerret[♠], Muriel Lansalot, Sylvain Marque, François Le Moigne , Hanns Fischer[§], Paul Tordo**

Aix-Marseille 1 & 3 Universities and CNRS, UMR 6517 "Chemistry, Biology and Free Radicals", Av. Normandie-Niemen, 13397, Marseilles Cédex 20, France
[♠] AtoFina, CRRA, rue Moissan, B.P. 63, 69310 Pierre-Bénite, France
[§] Physikalisch-Chemishes Institut der Universitat Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

Summary: Persistent nitroxides and their corresponding alkoxyamines are important regulators of living radical polymerization. Here we describe the synthesis of β-phosphorus nitroxides bearing a β-hydrogen, that present very interesting properties for the control of the radical polymerization of styrenes, acrylates and other monomers. A large series of alkoxyamines derived from these nitroxides was prepared, and Electron Spin Resonance (ESR) was used to determine both the temperature (T_c) and the rate constant (k_d) for their homolysis. For the whole series of alkoxyamines (27 compounds), a very good linear correlation was found between T_c and $\log k_d$. Satisfactory linear correlations were found between T_c and calculated (PM3 method) Bond Dissociation Energy (BDE) of the NO-C bond, for series of alkoxyamines with the same type of leaving radical. The characteristics of free radical polymerization of styrene carried out in the presence of these new nitroxides and alkoxyamines will be discussed.

Introduction

"Living"/Controlled free radical polymerizations can be performed through the reversible deactivation of growing polymeric radicals by stable radicals such as nitroxides.[1] One method to bring about "Living"/Controlled free radical polymerization is to use a conventional thermal initiator such as AIBN or BPO, along with commercially available nitroxides such as TEMPO.[2] A second method is to resort to alkoxyamines prepared beforehand which can be directly used to trigger polymerization. As a result of the so-called persistent radical effect,[3] both approaches share the same mechanistic concept. Growing polymeric radicals go through successive deactivation-dissociation cycles

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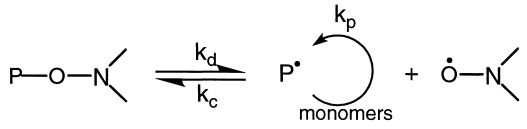
whereby they are alternatively transformed into alkoxyamines and reactivated by thermal homolysis (scheme 1).



Scheme 1: "Living"/controlled radical polymerization in presence of nitroxides.

The rate of polymerization in such systems depends on the constant of equilibrium K = k_d/k_c , and if K is too small, the rate of polymerization can be very sluggish and the control very poor.[4] The use of TEMPO to control the polymerization of styrene and derivatives results in a dramatic decrease of the rate of polymerization, even if the use of additives along with TEMPO allows these reactions to proceed faster.[5] Furthermore, TEMPO was shown to be ineffective in the control of acrylates and methacrylates. Other works have established that for different monomers, irreversible deactivation of the growing polymeric radical can occur through a dismutation reaction involving the nitroxide.[6] To overcome these limitations, the development of novel and more efficient nitroxides would be highly desirable.

Here we describe the synthesis of a new series of stable acyclic β-phosphorus nitroxides, which were found to efficiently control the polymerization of styrene and various monomers such as acrylates, acrylonitrile, acrylamide, diene… A large series of alkoxyamines derived from these new nitroxides has been prepared. Electron Spin Resonance (ESR) was used to determine both the temperature (T_c) and the rate constant (k_d) for the homolysis of these alkoxyamines. Applications of these new nitroxides and alkoxyamines to "living"/controlled free radical polymerization of styrene will also be discussed.

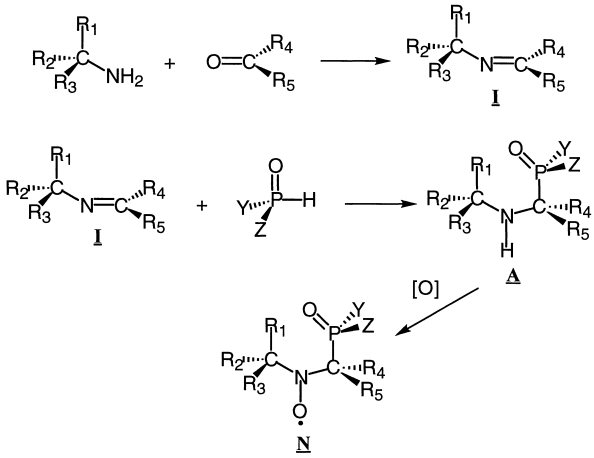
Synthesis of acyclic β-phosphorus nitroxides

The β-phosphorus nitroxides **N**, were obtained as shown in scheme 2. Addition of the appropriate phosphorus compound (YZP(O)H) to an imine (**I**) prepared in situ, led to amines (**A**) bearing a β-phosphorus group. Then, oxidation of **A** yielded the targeted

nitroxides. Using this synthetic approach, large amounts of nitroxides can be obtained and up to 100 kg of **N1** (routinely called SG1) were prepared. Oxidation of the corresponding aminophosphonate was carried out with peracetic acid, after the work up **N1** was 92% pure and the yield towards 2,2-dimethyl-propanal was 55 %.

Detailed experimental procedures have been already published,[7] and different characteristics of nitroxides prepared according to scheme 2 are shown in Table1.

When Y = Me, Z = EtO ; Y = Z = Me and Y = Z = *n*Pr the addition of YZP(O)H to 2,2-dimethyl-propanal was catalyzed with $BF_3.Et_2O$ (0.2 eq).



Scheme 2: General route for the synthesis of acyclic β-phosphorus nitroxides.

ESR study and stability of the nitroxides

Nitroxides bearing hydrogen atoms on the carbons adjacent to nitrogen (referred as β-hydrogens) usually decay through a self-reaction to yield a nitrone and a hydroxylamine.[8] Although they contain an H atom in β-position, at room temperature, nitroxides **N1** to **N11** are stable compounds which could be easily isolated and stored either neat or in solution. At higher temperature their half-life in organic solvents depends strongly on the steric strain. When the ethoxy groups of the phosphorus are replaced by Me or *n*Pr groups, the crowding around the phosphorus increases and a dramatic decrease of the half-life was observed (Table 1).

The β-couplings in β-phosphorus nitroxides follow simplified Heller, Mc Connell equations : $a_H = B_H \cos^2 \theta_H$ and $a_P = B_P \cos^2 \theta_P$[9], where θ_H is the dihedral angle between the planes N–Cα–Hβ and Cα–N–$2p_z$ whereas θ_P is the dihedral angle between the planes N–Cα–Pβ and Cα–N–$2p_z$, $2p_z$ being the principal direction of the $2p_z$

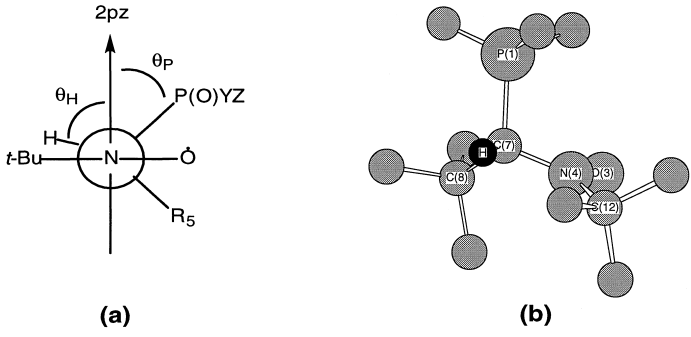


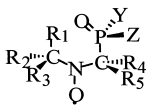
Figure 1: (a) major conformer of nitroxides **N1**-**N11**; (b) X-ray geometry of **N8**.

orbital of the nitrogen of the aminoxyl group (Figure 1a). For all the nitroxides included in Table 1 the β-hydrogen coupling was either unresolved or very small, in agreement with a θ_H value close to 90°. Moreover, the phosphorus coupling for **N1** is not temperature dependent and it is likely that in solution all these nitroxides adopt the conformation shown in Figure 1a (Y = Z = EtO; R_5 = *t*-Bu).[10] This conformation is in agreement with the X-ray geometry of **N2**[11] and that of **N8** shown on Figure 1b. In the favored conformer of nitroxides **N1**-**N11** the bulky substituents force the β-hydrogen (shown in black in Figure 1b) to stand close to the nodal plane of the aminoxyl group and hamper the self-reaction. For nitroxide **N8**, the very high steric crowding is reflected by the unusual large values of some bond lengths ($d_{P\text{-}C7}$ = 1.866 Å, $d_{C7\text{-}C8}$ = 1.57 Å) and some angles (C_7NC_{12} = 126.6°; PC_7C_8 = 115°).

The value of a_P decreases when the alkoxy substituents of phosphorus are replaced by methyl or *n*-propyl groups in nitroxides **N7**, **N8** and **N9**. According to the X-ray geometries , θ_P is almost the same for **N2** and **N8** , and the observed decrease of a_P can be

explained by a decrease of the P_{3s} character of the C-P bond, when the electronegativity of the phosphorus substituents decreases.[10,12]

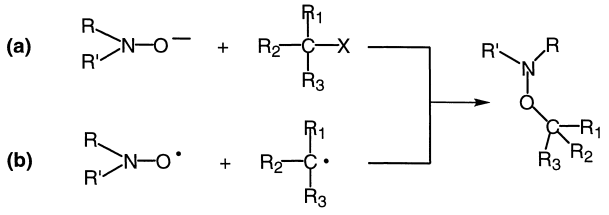
Table 1. Characteristics of some β-phosphorus nitroxides

Nitroxide 	Characteristics (Half-life ($t_{1/2}$) , 5 10^{-4} M in degassed *t*-BuPh)	ESR (5 10^{-4} M in *n*-hexane, in mT)
N1 $R_1 = R_2 = R_3 = Me$ R_5 = *t*-Bu, R_4 = H Y =Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C) 8 h (123 °C)	a_P = 4.62; a_N = 1.36 a_H : unresolved, g = 2.0061
N2 $R_1 = R_2 = R_3 = Me$ R_5 = *t*-Bu, R_4 = H Y =Z = $PhCH_2O$	Yellow solid mp : 90° C $t_{1/2} = \infty$ (25 °C) 8 h (123 °C)	a_P = 4.68; a_N = 1.36 a_H : unresolved, g = 2.0061
N3 $R_1 = R_2 = R_3 = Me$ R_5 = *i*Pr, R_4 = H Y =Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C)	a_P = 4.96; a_N = 1.39 a_H = 0.12; g = 2.0062
N4 $R_1 = R_2 = R_3 = Me$ R_5 = *cy*Hex, R_4 = H Y =Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C)	a_P = 5.00; a_N = 1.37 a_H = 0.13; g = 2.0061
N5 $R_1 = R_2 =$ Me, R_3 = H R_5 , $R_4 = (C H_2)_5$ Y =Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C)	a_P = 5.53; a_N = 1.36 a_H : unresolved, g = 2.0060
N6 R_1 ,$R_2 = (C H_2)_5$ R_3 = H, R_5 , $R_4 = (C H_2)_5$ Y =Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C)	a_P = 5.52; a_N = 1.35 a_H : unresolved, g = 2.0060
N7 $R_1 = R_2 = R_3 = Me$ R_5 = *t*-Bu, R_4 = H Y = EtO, Z = Me	Orange oil $t_{1/2} = \infty$ (25 °C) 9 h (90 ° C) 0.6 h (123 °C)	a_P = 3.86; a_N = 1.33 a_H : unresolved, g = 2.0059
N8 $R_1 = R_2 = R_3 = Me$ R_5 = *t*-Bu, R_4 = H Y = Z = Me	Orange solid mp : 115-116 ° C $t_{1/2}$ = 16 h (60 ° C) 0.5 h (90 ° C)	a_P = 3.22; a_N = 1.32 a_H : unresolved, g = 2.0063
N9 $R_1 = R_2 = R_3 = Me$ R_5 = *t*-Bu, R_4 = H Y = Z = *n*Pr	Yellow solid mp : 93 ° C $t_{1/2}$ = 1 h (60 ° C)	a_P = 3.33; a_N = 1.30 a_H : unresolved, g = 2.0063
N10 $R_1 = R_2 = Me$ $R_3 = CH_2OH$ R_5 = *t*-Bu, R_4 = H Y = Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C) 8 h (123 °C)	a_P = 3.99; a_N = 1.37 a_H : unresolved, g = 2.0063
N11 $R_1 = R_2 = R_3 = Me$ R_4 = H $R_5 = C(CH_3)_2CH_2OC(O)nC_7H_{15}$ Y = Z = EtO	Orange oil $t_{1/2} = \infty$ (25 °C) 8 h (123 °C)	a_P =4.71; a_N = 1.36 a_H : unresolved, g = 2.0061

Synthesis of alkoxyamines

In "living"/controlled radical polymerizations, a sufficiently large k_d (Scheme 1) is required to ensure reasonable conversion times and low polydispersities. However, k_d must not exceed a critical value for which the controlling persistent radical effect breaks down, and the optimum values for k_d and k_c depend on the propagation and termination rate constants.[4] It would be helpful if k_d could be reasonably predicted based on alkoxyamine and nitroxide structure to avoid unnecessary synthetic and experimental work. To test the possibilities offered by our series of β-phosphorus nitroxides, we used them to prepare a large variety of low molecular model alkoxyamines, with representative substitutions of the alkyl moiety (Tables 2 and 3). For comparison, some alkoxyamines derived from TEMPO and 2,2,5,5-tetramethyl-4-phenyl-3-azahexane-3-oxyl (TIPNO)[12] were also prepared.

Most of the alkoxyamines of interest for "living"/controlled radical polymerization are prepared either by reacting the sodium salt of the corresponding nitroxide with the appropriate alkyl halide[13] (Scheme 3a) or by a coupling reaction between a nitroxide and a free radical (scheme 3b).[14]

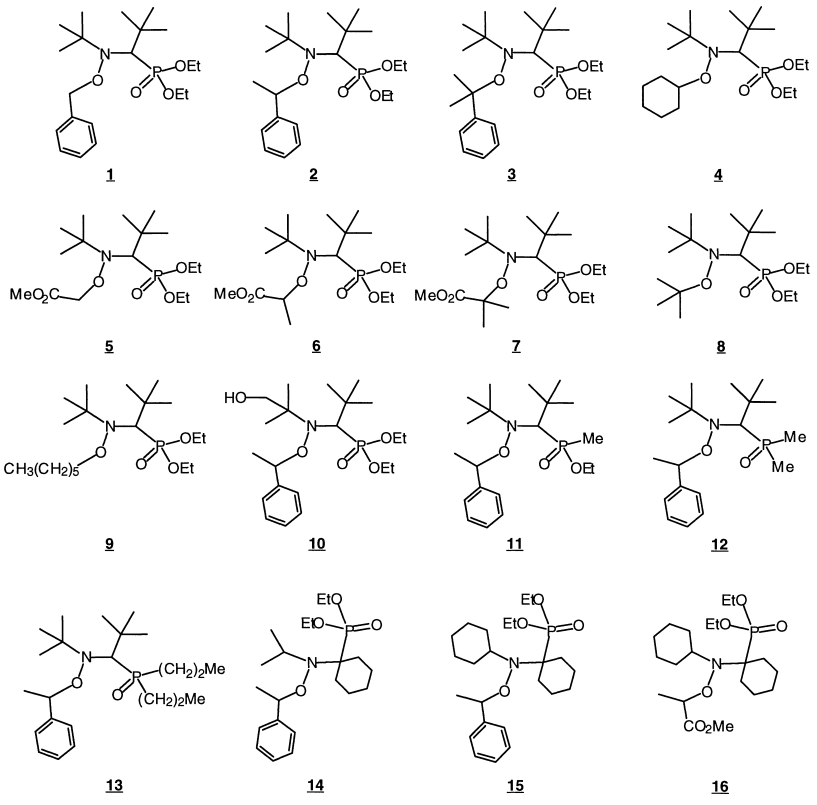


Scheme 3: Synthesis of alkoxyamines.

Depending on the nature of the alkyl radical $R_1R_2R_3C^{\bullet}$, different modes of radical generation have been used.[15] All the alkoxyamines displayed in Tables 2 and 3 have been prepared via the trapping of free radicals with nitroxides. Yields for isolated compounds, were close or above 80%. Compounds **3** and **7** were characterized only in solution and could not be isolated since the cleavage of their C-ON bond occurs below room temperature.

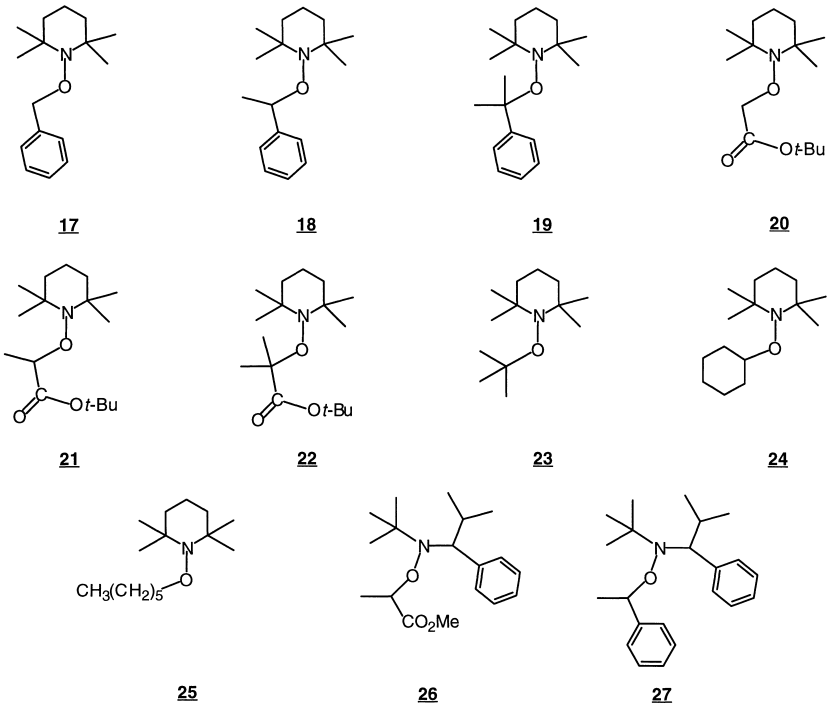
Apart **8**, **23**, **4**, **24**, **9** and **25** all the other alkoxyamines have been synthezised according to a method derived from atom transfer radical polymerization (ATRP), and first reported by Matyjaszewski.[16] In this method, the radicals R• are generated via copper (I) reduction of the corresponding organic halides RX.

Table 2. Prepared alkoxyamines derived from β-phosphorus nitroxides



Owing to the facile homolysis of most of the prepared alkoxyamines, their synthesis was carried out at room temperature. To obtain the complete conversion of nitroxides excess of copper (I) (2 eq.) and alkyl halides (2 eq.) was necessary. In our experimental conditions, we found that addition of 1 equivalent of copper (0) slightly improved the yield and the reaction time. For **8**, **23**, **4**, **24**, **9** and **25** the radicals R• have been generated through oxidation of the correponding organometallic compound with 1 equivalent of nitroxide.

Table 3. Prepared alkoxyamines derived from TEMPO and TIPNO



17 18 19 20 21 22 23 24 25 26 27

Alkoxyamines **8**, **23**, **4**, and **24**, have been prepared by reacting 1 equivalent of *tertio*-butyl magnesium bromide or cyclohexylmagnesium bromide with 2 equivalents of either **N1** or TEMPO at -78°C in anhydrous THF. Alkoxyamines **9** and **25**[17] have been obtained by treating 2 equivalents of nitroxide with 1 equivalent of *n*-hexyl lithium at -78°C in THF.

Characteristics of alkoxyamine homolysis : ESR investigation

In successful living radical polymerization, k_d is sufficiently large to ensure reasonable conversion times and low polydispersities. However, k_d must not exceed a critical value for which the controlling persistent effect breaks down.[4] As a rule, $k_d \geq 10^{-3}\ s^{-1}$ is desirable and it would be helpful if k_d could either be rapidly estimated or predicted based on alkoxyamine and nitroxide structure. To examine these possibilities we

prepared a large series of model alkoxyamines and for each molecule we calculated the BDE of the NO-C bond, and we used ESR to measure k_d and the temperature of cleavage T_c.

k_d measurements : As shown in scheme 1 due to the reformation of the alkoxyamine, k_d cannot be taken directly from its decay under normal conditions. Instead, conditions have to be chosen such that the transient radicals are rapidly and completely converted to other unreactive species before reformation of the alkoxyamine can occur. We and other have previously shown[18,19] that k_d can be measured by ESR monitoring of the nitroxide build-up, using dioxygen, galvinoxyl radical or TMIO-$^{15}ND_{12}$ (2,2,10,10-tetraperdeuteriomethylisoindolin-^{15}N-oxyl) as scavengers for the transient radicals. The experiments were carried out in *tert*-butylbenzene, and the rate constants k_d were measured using either the plateau (P method, eq. 1) or the initial slope (IS method, eq. 2) of the curve giving the time dependence of the nitroxide concentration.

$$\ln\left(\frac{[\text{nitroxide}]_\infty - [\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}\right) = -k_d t \qquad \text{eq. 1}$$

$$[\text{nitroxide}]_t/[\text{nitroxide}]_\infty = k_d t \qquad \text{eq. 2}$$

The activation parameters and rate constants for the dissociation of alkoxyamines **1** to **27** are listed in Tables 4 and 5, respectively. Results were reproducible, and rate constants do not change upon varying the alkoxyamine concentration. We have previously shown, that the frequency factor A for the C-ON bond homolysis of alkoxyamines (24 different compounds studied) does not vary much with alkoxyamine structure and lies between 10^{13} and 10^{15} s^{-1}, with an average value of $2.4 \cdot 10^{14}$ s^{-1}.[18,20] When the dissociation rate constant was determined at a few temperatures, this average value was used to estimate E_a. The estimated E_a values listed in Table 4 were averaged over the measured temperature range.

For **4**, **5** and **9**, the rate constant and the E_a values may suffer of larger error, because at high temperature **N1** is less persistent and the measures were performed at very low alkoxyamine conversion (<5 %).

Table 4. Activation parameters at 120 °C for the dissociation of alkoxyamines **1** to **27**

Alkoxyamine[a]	Runs	T /°C	Methods[b]	$A^{c}/10^{14}\cdot s^{-1}$	E_a^{d} /kJ·mol^{-1}	ref.
1	3	110 - 131	P and IS	(2.4)	136.2	[18]
2	20[e]	60 -137	P and IS	1.9	124.5	[18]
4	1[f]	150	IS	(2.4)	162.3	this work
5	3[g]	130 - 150	IS	(2.4)	149.1	this work
	12[h]	80 - 132	P and IS	3.5	128.4	
6						[18]
	4[i]	90 - 129	P	(2.4)	130.8	
8	3[j]	120 - 140	P and IS	(2.4)	139.7	this work
9	1[k]	150	IS	(2.4)	169.2	this work
10	3[l]	90 - 120	P	(2.4)	121.0	[18]
11	11[m]	60 - 119	P	0.5	115.0	[18]
	3[h]	80 - 121	P	(2.4)	118.2	
12						[18]
	3[i]	80 - 100	P	(2.4)	116.7	
14	3	101 -121	P	(2.4)	126.3	[18]
15	13	60 - 131	P	2.9	126.2	[18]
17	2	131 - 150	P	(2.4)	145.5	[18]
18	17	90 - 150	P	2.5	133.0	[18]
19	9	70 - 92	P	2.0	115.7	[18]
20	2	151	IS	(2.4)	161.5	[18]
21	11	90 -151	P and IS	1.0	139.0	[18]
22	16	65 - 121	P	1.8	119.8	[18]
23	3	130 - 151	P and IS	(2.4)	145.8	[20]
24	1	151	IS	(2.4)	165.1	[18]
26	6[n]	110 - 130	P and IS	(2.4)	133.4	this work
27	10[o]	60 - 131	P	5.6	129.6	[18,20]

a) [Alkoxyamine] = 10^{-4} M unless otherwise mentionned. b) P : plateau method (see eq. 1) and IS : initial slope method (see eq. 2). c) Statistical errors smaller than a factor of 2. Value in brackets is the average of all experimentally accessible frequency factors in [18, 20]. d) Statistical errors between 2 and 3 kJ·mol^{-1}. e) Both diastereoisomers exhibit the same rate constant. f) [alkoxyamine] = 10^{-2} M; at 0.2% conversion. g) [alkoxyamine] = $1.2\cdot10^{-2}$ M, 10^{-3} M and $1.2\cdot10^{-3}$ M; at 5% conversion. h) Isomer RS/SR. i) Isomer RR/SS. j) [alkoxyamine] = $2\cdot10^{-3}$ M for the IS method. k) [alkoxyamine] = $2\cdot10^{-2}$ M; at 0.05% conversion. l) 70:30 mixture (^{1}H NMR) of diastereoisomers, unimodal decay. m) One diastereoisomer of unknown configuration. n) One pure diastereoisomer and a mixture of diastereoisomers showed the same rate constants. o) 2:1 mixture (^{1}H NMR) of diastereoisomers, unimodal decay.

T_c measurements : A precise protocol was followed to determine the cleavage temperature, T_c, for our series of alkoxyamines. Two ESR tubes were filled with 0.01 M *tert*-butylbenzene solution of alkoxyamine and degassed with several freeze-pump-thaw cycles. With the first sample, a rough estimation of T_c was made. The temperature was increased stepwise by 5 °C and the rough T_c corresponds to the temperature where either the ESR signal of the nitroxide appears or increases significantly (for some alkoxyamine a small nitroxide signal is already present at room temperature). Then, the second probe is inserted in the ESR cavity preheated at 30 °C below the rough T_c.

Table 5. Temperature of cleavage, T_c, homolysis rate constant,[a] k_d, and calculated [b] BDE of the C-ON bond, for alkoxyamines **1** to **27**

Alkoxyamines	T_c /°C	k_d /s^{-1}(120 °C)	BDE(C-O) /kJ·mol^{-1}
1	80	$3.3 \cdot 10^{-4}$	153.6
2	60	$5.5 \cdot 10^{-3}$	111.3,[c] 117.2 [d]
3	≈ 15 ± 5	-	71.1
13	35	-	-
17	115	$1.1 \cdot 10^{-5}$	159.4
18	95	$5.2 \cdot 10^{-4}$	129.3
19	45	$8.5 \cdot 10^{-2}$	103.8
27	65	$3.3 \cdot 10^{-3}$	106.7,[d] 112.1 [c]
5	100	$3.6 \cdot 10^{-6}$	-
6	75	$3.0 \cdot 10^{-3}$ [d] 10^{-3} [c]	103.3,[c] 105.9[d]
7	≈ 15 ± 5	-	58.6
20	145	$8.1 \cdot 10^{-8}$	142.7
21	115	$3.4 \cdot 10^{-5}$	112.5
22	50	$2.2 \cdot 10^{-2}$	81.6
26	90	$4.5 \cdot 10^{-4}$	114.6
4	140	$6.4 \cdot 10^{-8}$	119.2
8	95	$6.5 \cdot 10^{-5}$	73.6
9	160	$8.0 \cdot 10^{-9}$	145.6
23	110	10^{-5}	93.3
24	170	$< 2.8 \cdot 10^{-8}$	127.6

[a]Estimated from A and E_a given in Table 4. [b] BDE(SG1-R), BDE(TIPNO-R) and BDE(TEMPO-R) were calculated using PM3 approximation [23] [c] Isomer RR/SS. [d]Isomer RS/SR.

The temperature is increased stepwise by 5°C, and T_c corresponds to the temperature where the ESR signal recorded at close intervals (1 to 2 min) showed a steadily increase.

Discussion : Previous work[18] and data of tables 4 and 5 clearly show that the activation energies of alkoxyamine dissociations depend strongly on the structure of the leaving transient radical and on the structure of the nitroxide. Whatever the leaving radical the homolysis of the alkoxyamines derived from **N1** exhibited the lowest activation energy and the highest k_d. This result is in agreement with the observed higher efficiency of **N1** to control free radical polymerizations of styrene and different acrylic monomers.[7]

A very good linear correlation (eq. 3) was found (Figure 2) between k_d and T_c for all the alkoxyamines listed in Tables 2 and 3.

$$\log k_d = - 0.057\ T_c + 1.48 \qquad \text{eq. 3}$$

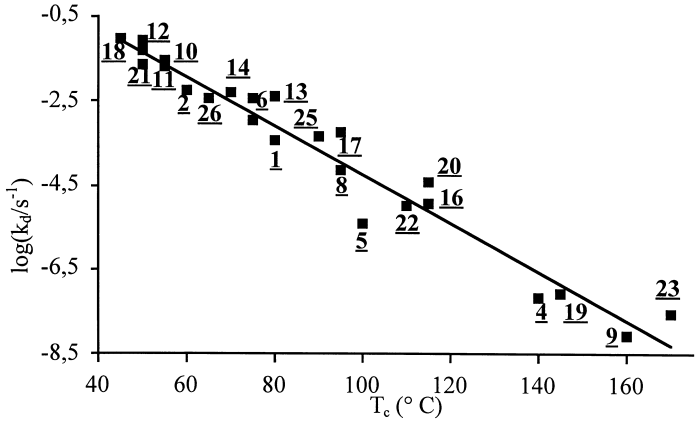


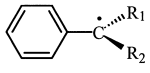
Figure 2: Plot of $\log k_d$ versus T_c for alkoxyamines **1** to **27**.

This result shows that for a newly prepared model alkoxyamine, ESR measurement of T_c is a simple way to rapidly estimate its k_d and its potential for controlled radical polymerization.

Alkoxyamine **3** is decomposed slowly at room temperature and its Tc can be estimated to be 15 ± 5 °C. Then, using equation 3 and the previously mentionned average value ($2.4\ 10^{14}\ s^{-1}$) for the frequency factor A, activation energy E_a of **3** at 120 °C is 102.2 ±

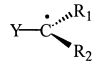
1.3 kJ/mol . If we compare E_a for **1**, **2** and **3** we can see that the introduction of one methyl group in leaving radical decreases E_a by –12 kJ/mol, while the introduction of a second methyl decreases E_a by –22 kJ/mol. This result shows that steric effects exert a strong influence on the rate of alkoxyamine dissociation. In the corresponding TEMPO series (alkoxyamines **17** , **18** and **19**), a smaller steric strain is expected and the introduction of the second methyl group induces a lower E_a decrease (– 17 kJ/mole).

The combination of carbon-centered radicals with nitroxides (scheme 1), is usually fast $k_c \geq 10^7$ $M^{-1}s^{-1}$and shows little temperature dependence.[21]. Hence, the activation energies E_a must be close to the NO-C bond dissociation energies (BDE). We have calculated such energies by density functional theory for a few alkoxyamines considered in this report.[22] We found 144 $kJ.mol^{-1}$ for **17**, 130 $kJ.mol^{-1}$ for **18**, 108 $kJ.mol^{-1}$ for **19**, 135 $kJ.mol^{-1}$ for **1** and 120 $kJ.mol^{-1}$ for **2**, whereas the activation energies are 145.5, 133, 115.7, 136.2 and 124.5 $kJ.mol^{-1}$. Considering the unknown but small barrier for the combination reaction, the two data set agree very well. However, DFT calculations on large molecules are rather tedious and the BDE listed in Table 5 were determined using the PM3 semi-empirical method.[23] When the whole series of alkoxyamines listed in Tables 2 and 3 was considered, no linear correlations were found between T_c or $\log k_d$ and BDE(C-O). However, satisfactory linear correlations were found if we consider three series of alkoxyamines characterized by the nature of the leaving radical (scheme 4).



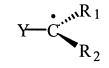
R_1 , R_2 = H or Me

BDE = 0.85 T_c + 62.1 ; R^2 = 0.85



R_1 , R_2= H or Me, Y = CO_2R

BDE = 0.61 T_c + 52.3 ; R^2 = 0.95



R_1 , R_2 and R_3 = H or alkyl

BDE = 0.83 T_c - 0.93; R^2 = 0.91

Scheme 4: Correlations between BDE and T_c for different series of alkoxyamines.

This result indicates that the PM3 method is not appropriate to estimate the trend of the heat of formation within a series of alkyl radicals bearing substituents with very different electronic effects. However, for an homogeneous series of alkyl radicals, PM3 can be a fast and cheap method to investigate some molecular characteristics of derived alkoxyamines.

"Living"/Controlled polymerization of styrene

Polymerization of styrene in the presence of alkoxyamine 6. The efficiency of this alkoxyamine was already described[7, 24, 25] for the synthesis of living polystyrene up to Mn = 50 kg.mol^{-1}. However, for industrial applications, polystyrene of higher molecular weight (Mn close to 80 – 120 kg.mol^{-1}), is often needed. We have examined the possibility to prepare living polystyrene of high molecular weight in the presence of **6**. To decrease the influence of the viscosity, experiments were carried out in a solvent (ethylbenzene : often used in industrial plants), and targeted molecular weights were 400, 220, 110 and 22 kg.mol^{-1}.

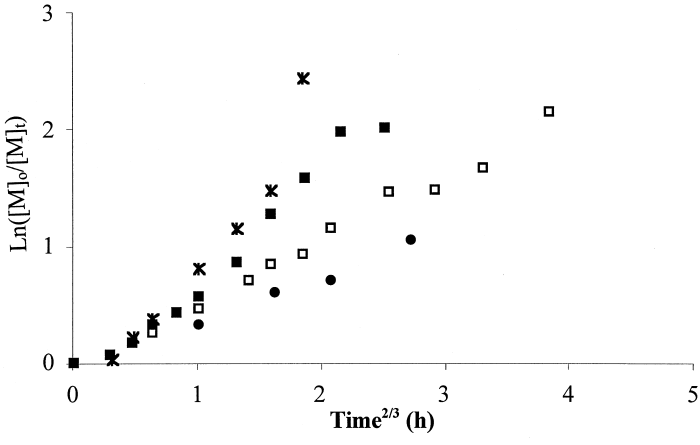


Figure 3: Kinetic plots of Ln ($[M]_0/[M]$ versus $t^{2/3}$ for the polymerization of styrene with **6** ; experimental conditions : T = 130°C, styrene/ethylbenzene (70/30 per weight), ● [**6**] =2.1x10^{-3} mol.L$^{-1}_{Styrene}$; □ [**6**] = 4.2x10^{-3} mol.L$^{-1}_{Styrene}$; ■ [**6**] = 8.4x10^{-3} mol.L$^{-1}_{Styrene}$; ∗ [**6**] = 4.2x10^{-2} mol.L$^{-1}_{Styrene}$.

The effect of the initial concentration of **6** on the kinetic of polymerization is shown in Figure 3. In all cases, the polymerization rate was fast and increased when the concentration of **6** increased. The polymerization time was much shorter than that observed for the same experiments carried out with alkoxyamines derived from TEMPO (4 h instead of more than 24 h).

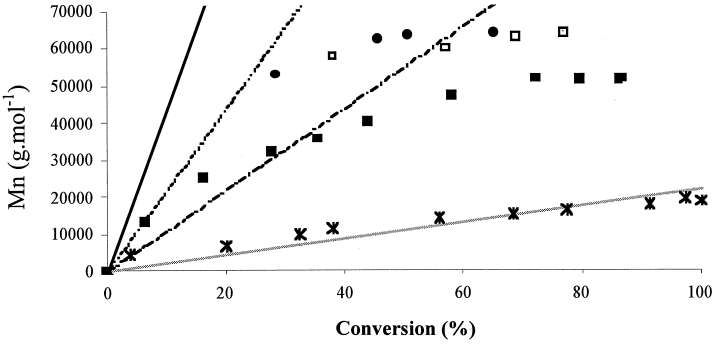


Figure 4: Mn (GPC in THF at 40°C) for the polymer fraction as a function of conversion ; experimental conditions : T = 130°C, styrene/ethylbenzene (70/30), ● [**6**] = $2.1x10^{-3}$ $mol.L^{-1}_{Styrene}$ (—— theoretical evolution) ; □ [**6**] = $4.2x10^{-3}$ $mol.L^{-1}_{Styrene}$ (- - - theoretical evolution) ; ■ [**6**] = $8.4x10^{-3}$ $mol.L^{-1}_{Styrene}$ (- —— theoretical evolution) ; ∗ [**6**] = $4.2x10^{-2}$ $mol.L^{-1}_{Styrene}$ (—— theoretical evolution).

However, as shown on Figure 4, the targeted high molecular weights were not reached. Moreover, the final number average molecular weight, Mn, was not dependent on the initial concentration of alkoxyamine, and plateaued around 65000 $g.mol^{-1}$. This result indicates that the number of chains was greater than the theoretical number predicted according to eq. 4.

$$Mn_{th} = \frac{conversion.[M]_0.MM_{styrene}}{[chains]_{th}} \qquad \text{eq. (4)}$$

with
Mn_{th} : theoretical number average molecular weight ($g.mol^{-1}$)
$[M]_0$: initial monomer concentration ($mol.L^{-1}_{styrene}$)
$MM_{styrene}$: styrene molecular weight (104 $g.mol^{-1}$)
$[chains]_{th}$: chain concentration ($mol.L^{-1}_{styrene}$)

If, for a given conversion, the experimental molecular weight is smaller than the theoretical one, then : $[chains]_{exp} = [chains]_{th} + [X]$, where [X] is the concentration of "additional " chains which are not produced from the alkoxyamine. The estimated values of [X], after 2h 30 of reaction are listed in Table 6. The proportion of these additional chains increased when the initial alkoxyamine concentration decreased, and the same results were obtained in the absence of ethylbenzene.

In our experimental conditions the formation of these additional chains from thermal polymerization is the most likely. Different approaches[26-27] were suggested to decrease the influence of thermal polymerization of styrene but none is very efficient. In order to reduce the amount of thermal chains we first carried out polymerization at lower temperature (110°C instead of 130°C). However, the polymerization time was then

Table 6. Concentration of "additional" chains X , after 2h 30 of reaction

Expt.	$[chains]_{th}$ $mol.L^{-1}_{St}$	Conversion %	M_n th $g.mol^{-1}$	M_n exp $g.mol^{-1}$	$[chains]_{exp}$ $mol.L^{-1}_{St}$	[X] $mol.L^{-1}_{St}$	$[X]/[Chains]_{exp}$ %
*	$4.2.10^{-2}$	91.3	20 100	17 900	$4.6.10^{-2}$	$4.6.10^{-3}$	10
■	$8.4.10^{-3}$	79.7	87 700	51 500	$1.4.10^{-2}$	$5.7.10^{-3}$	41
□	$4.2.10^{-3}$	60.5	133 100	62 000	$8.2.10^{-3}$	$4.0.10^{-3}$	49
●	$2.1.10^{-3}$	48.0	211 200	61 000	$6.8.10^{-3}$	$4.7.10^{-3}$	70

considerably increased (Figure 5), and as shown on Figure 6, the proportion of thermal chains was even higher than in the previous experiments.

An alkoxyamine with a higher k_d than **6**, should allow to control styrene polymerization and perform the polymerization in a reasonnable time. We have already shown[7] that in the presence of alkoxyamines **12** and **13** (Table 2), low molecular weight polystyrenes (Mn up to 30 $kg.mol^{-1}$) with low polydispersity (close to 1.2-1.3) could be obtained at temperatures below 100 °C. For a polymerization of styrene at 95 °C in the presence of **12** (0.044 M, Mn_{th} = 20.6 $kg.mol^{-1}$), 85 % conversion was reached after 3.5 h and the polydispersity was 1.27. Hence, we decided to investigate the possibilities offered by **12** to prepare hight molecular weight living polystyrene.

Polymerization of styrene in the presence of 12. At 120 °C k_d for **12** is 20 times faster than for **6**, and T_c is 25 °C lower. When a polymerization of styrene was conducted in the presence of **12** at 110 °C the trend of experimental molecular weights versus conversion was almost the same (Figure 7) than in the presence of **6**. However,

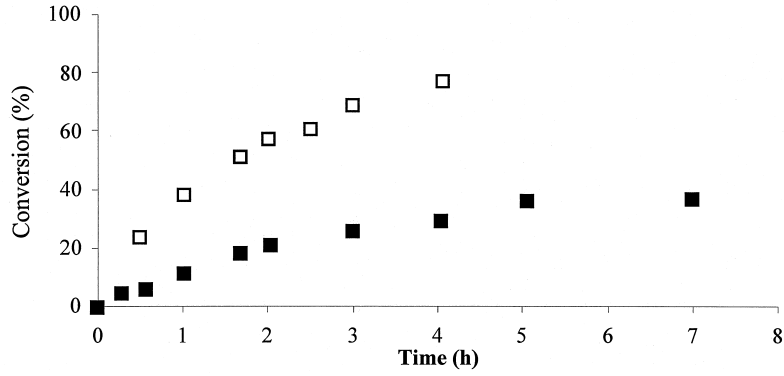


Figure 5: Conversion versus time for the polymerization of styrene with alkoxyamine **6**; experimental conditions : [**6**] = ($4.2x10^{-3}$ $mol.L^{-1}_{Styrene}$), styrene/ethylbenzene (70/30 per weight), □ = T : 130°C ; ■ = T : 110°C.

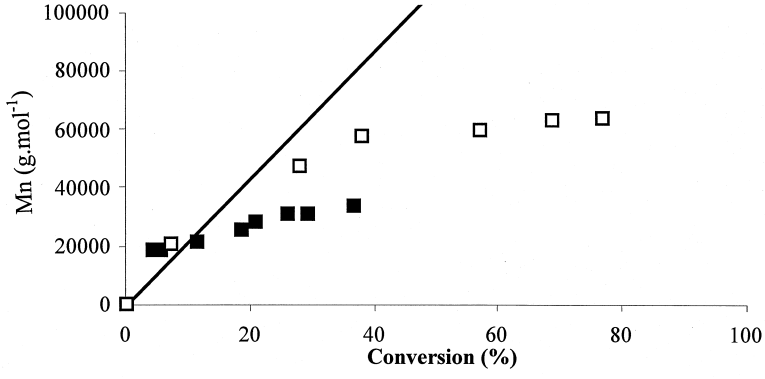


Figure 6: Mn of the polymer fraction as a function of conversion ; experimental conditions : $[\mathbf{6}]_0 = 4.2x10^{-3}$ $mol.L^{-1}_{Styrene}$, styrene/ethylbenzene (70/30), □ = T : 130°C ; ■ = T : 110°C ; (— theoretical evolution).

after 4 h the conversion had reached a plateau close to 40 % (figure 8). When the same reaction was repeated at 95 °C the conversion limit was slightly improved (50 % after 200 min) but Mn plateaued at 50 $kg.mol^{-1}$. The poor stability of the nitroxide **N8** released by homolysis of **12** could explain the above results. If we consider only the homolysis of dormant species **12**-P, and the combination of **N8** with polymer radicals P•, the average lifetimes of **N8** and **12** in the reaction mixture can be written as:

$$\tau_{\mathbf{N8}} = [\mathbf{N8}] / (k_{rec}.[\mathbf{N8}].[P]) \text{ and } \tau_{\mathbf{12}} = [\mathbf{12}]/(k_d.[\mathbf{12}])$$

where [P] is the polymer concentration ($\approx 3\ 10^{-8}$ mol.L^{-1}), and $k_{rec} \approx 5\ 10^{5}$ L.mol^{-1}.s^{-1} , $k_d = 2.10^{-2}$ s^{-1} are the rate constants for the reformation and the cleavage of **12**-P, respectively.

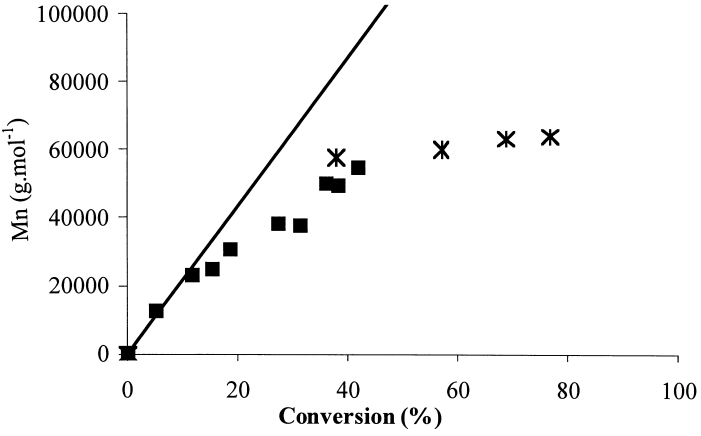


Figure 7: Mn for the polymer fraction as a function of conversion ; experimental conditions : $[alkoxyamine]_0 = 4.2x10^{-3}$ mol.L^{-1}$_{Styrene}$, styrene/ethylbenzene (70/30), * = **6**, T : 130°C ; ■ = **12**, T : 110°C, (— theoretical evolution).

With these values, the average lifetime for **N8** is 70 s, whereas the average lifetime for **12** is 50 s. For the polymerization conducted in the presence of **12** at 110°C, the reaction time to reach the plateau was close to 4 hours (14400 s). Then, the average global lifetime of **N8** is 8400 s, and as its corresponding chemical half-life time is close to 250 s, after 4 hours all the nitroxide has been decomposed, and only dead polymer chains are produced.

Polymerization of styrene in the presence of 13. The cleavage temperature (T_c) for **13** is 35°C, and polymerization of styrene was carried out at 75°C. At this temperature the half-life time of **N9** is close to 1000 s, and it should exert a better control of the polymerization than **N8** . Indeed, we observed that as with the alkoxyamine **6**, the rate of polymerization was dependent on the alkoxyamine concentration. Moreover, even when high molecular weight polystyrene was targeted (100 kg.mol^{-1}), a linear increase

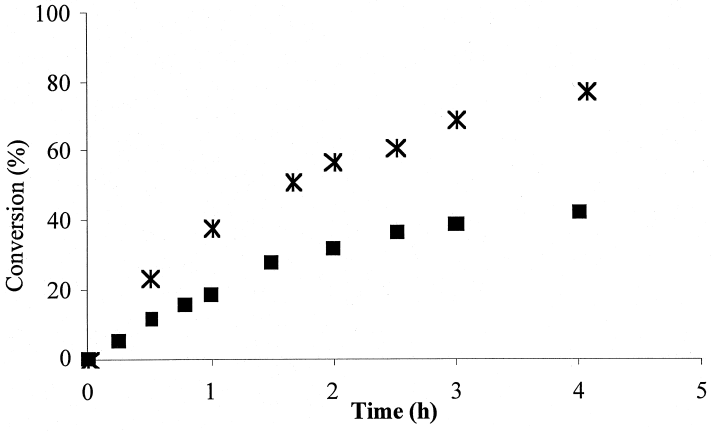


Figure 8: Conversion versus time for the polymerization of styrene with **12**; experimental conditions : $[alkoxyamine]_0 = 4.2x10^{-3}$ $mol.L^{-1}_{Styrene}$, styrene/ethylbenzene (70/30 per weight), ∗ = **6** , T : 130°C ; ■ = **12**, T : 110°C.

of Mn and Ln $[M]_o/[M]$ versus time was observed, up to 80 % of conversion. Finally, the experimental Mn were close to the theoretical values.

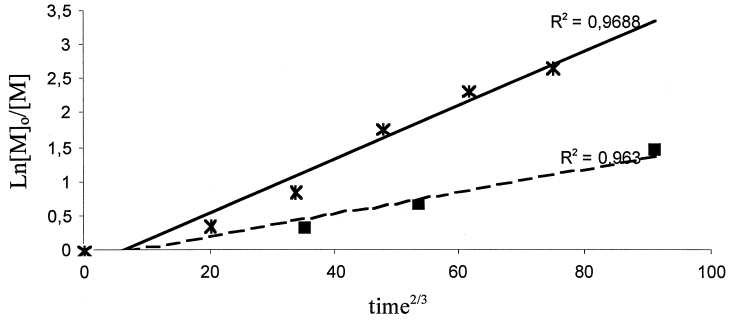


Figure 9: Ln $([M]_o/[M]$ versus $time^{2/3}$ for the polymerization of styrene with **13** ; experimental conditions : T = 75°C, ■ [**13**] = $8.4x10^{-3}$ $mol.L^{-1}_{Styrene}$; ∗ [**13**] = $4.2x10^{-2}$ $mol.L^{-1}_{Styrene}$.

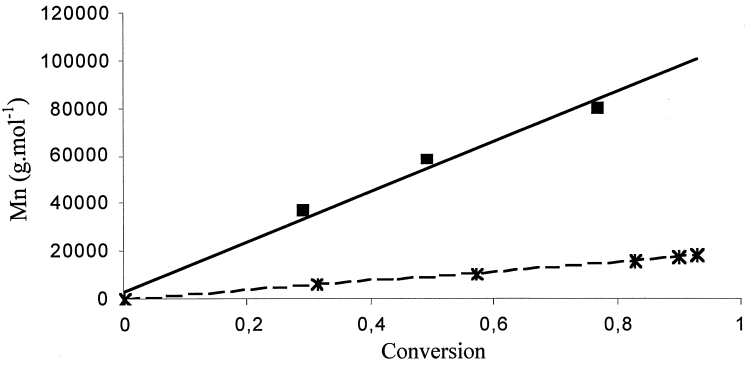


Figure 10: Mn as a function of conversion for the polymerization of styrene with **13**; experimental conditions : : T = 75°C, ■ [**13**] = 8.4×10^{-3} $mol.L^{-1}_{Styrene}$; ∗ [**13**] = 4.2×10^{-2} $mol.L^{-1}_{Styrene}$.

Conclusion

A series of novel linear β-phosphorus nitroxides and derived model alkoxyamines were prepared for the control of free radical polymerizations. Using ESR, an easy method was designed to determine the temperature of cleavage (T_c) of alkoxyamines. For the series of alkoxyamines derived from **N1**, T_c was lower by 30-40 °C compared to the TEMPO analogues. ESR was also used to determine the kinetics of the C-O bond cleavage. We found a correlation by which rate constants for the C-O bond cleavage of an alkoxyamine can be predicted from its T_c value.

In the presence of **6**, as a result of autopolymerization, living polystyrenes with Mn higher than 40-50 $kg.mol^{-1}$ cannot be obtained. With the use of **12** (T_c = 50 °C), polymerization of styrene can be carried out at 95 °C. However, at this temperature the nitroxide **N8** is too rapidly decomposed through unimolecular decay, and only dead polymer chains were obtained.

The use of alkoxyamine **13** (T_c = 35 °C) afforded interesting preliminary results. At 75 °C the polymerization of styrene was well controlled. Linear increase of Mn and Ln $[M]_0/[M]$ versus time was observed up to 80 % of conversion which was obtained after 14 hours. No plateau was observed for Mn which reached a value of 80 $kg.mol^{-1}$ for a targeted value of 100 $kg.mol^{-1}$.

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