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Nitroxide-Mediated Living Radical Polymerization: Determination of the Rate Coefficient for Alkoxyamine C−O Bond Homolysis by Quantitative ESR

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ABSTRACT: The rate coefficient for alkoxyamine C−O bond homolysis has been determined over a range of temperatures for both 2-*tert*-butoxy-1-phenyl-1-(1-oxy-2,2,6,6-tetramethylpiperidinyl)ethane (**1**) and a polystyrene−TEMPO (approximately 75 units) adduct using quantitative ESR. In a thermostated solution of the alkoxyamine species in toluene the nitroxide concentration was monitored via ESR. Measurements were performed under atmospheric conditions to create pseudo-first-order kinetics with oxygen to serve as a scavenger for the carbon-centered radicals. The acquired kinetic data for alkoxyamine **1** were compared with data obtained via nitroxide-exchange experiments using HPLC to monitor the alkoxyamine concentrations. The data for the polystyrene alkoxyamine were compared with literature data obtained by Fukuda via his GPC method. The quantitative ESR measurements proved to be an easy and more important an accurate method to determine values for the rate coefficient for alkoxyamine C−O bond homolysis. The Arrhenius parameters obtained via this method were $A = 1.1_0 \times 10^{14}$ s^{-1} and $E_{act} = 133._2$ kJ mol^{-1} for alkoxyamine **1** and $A = 1.0_2 \times 10^{16}$ s^{-1} and $E_{act} = 140._9$ kJ mol^{-1} for its polymeric analogue.

Introduction

The alkoxyamine C−O bond is known to be relatively unstable.[1−3] Upon heating, it readily cleaves homolytically to yield a carbon-centered radical species and a nitroxide. Directly related to this homolysis is the process of trapping a carbon-centered radical with a nitroxide. This generally occurs via coupling of the two species to yield the alkoxyamine as a covalent adduct. In this way, the alkoxyamine homolysis can be considered as a reversible process. (Note that in this paper the alkoxyamine, carbon-centered radical and nitroxide may be represented by the symbols L, R$^•$, and T$^•$, respectively.)

This reversible homolytic C−O bond cleavage of alkoxyamines has led to the development of a living-radical polymerization technique.[4,5] In terms of a nitroxide-mediated living-radical polymerization, this so-called reversible activation of the dormant alkoxyamines needs to meet two basic requirements. First, the alkoxyamine C−O bond homolysis needs to produce a carbon-centered radical that is able to undergo addition to monomer (propagation). Second, the nitroxide needs to be a persistent compound, which is only capable of trapping the carbon-centered radical via coupling, preferably at a diffusion-controlled rate.

In this paper we will focus on the determination of the rate coefficient for the homolytic alkoxyamine C−O bond cleavage (k_{ed}/s^{-1}). A more thorough discussion on the reversible and nonreversible homolysis of alkoxyamine species and the implications to the living-radical polymerization process will follow in two subsequent papers.

The Determination of k_{ed}

There are two versatile methods to determine correct values of k_{ed}. The first method involves an enantiomerically pure alkoxyamine having a chiral center at its nitroxide-substituted carbon atom. After homolysis, R$^•$ will lose its specific sp^3 hybridized configuration. If no stereospecific trapping occurs, the rate of racemization is a measure of the rate for alkoxyamine homolysis. This method, however, is not studied in the work presented here.

The second, and most evident, method is to react the generated R$^•$ with a disparate compound. In general, pseudo-first-order conditions are created, to ensure that the only fate of R$^•$ is to react with this compound. We will now shortly mention examples from the literature, which use an excessive amount of a different nitroxide, molecular oxygen, and monomer to acquire rate data under pseudo-first-order conditions. The added compounds will be referred to as “scavenger” for clarity.

Solomon et al.[4] and, more recently, Scaiano and coworkers[6] reported half-life measurements on a variety of alkoxyamine species in the presence of a large excess of a different nitroxide. In these so-called nitroxide-exchange experiments the ratio of the two alkoxyamine species present in the system is measured after a certain period of time (by HPLC) to obtain the data for the rate coefficient for homolysis (k_{ed}).

In the late 1970s Howard[2,7] reported in exploratory studies the monitoring of the nitroxide production via quantitative ESR measurements on solutions of certain alkoxyamines in the presence and absence of oxygen, as measures of the homolytic C−O bond cleavage. Similar experiments to yield apparent values for k_{ed} were performed by Veregin et al.[8]

Fukuda and co-workers[9] showed that k_{ed} values could be obtained for alkoxyamine (**2**, with $\langle M_n \rangle = 1.7 \times 10^3$ g mol^{-1}, $\gamma = 1.11$, and $P_{dead} = 5\%$) from a true nitroxide-mediated living radical polymerization system, i.e., in the presence of monomer, by means of GPC analysis. The essence of this method is that R$^•$ is forced to propagate multiple times as a result of an additional

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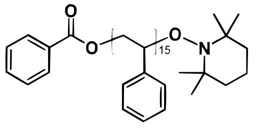
radical flux created by addition of *tert*-butyl hydroperoxide to the system.



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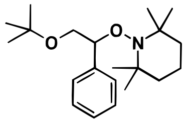

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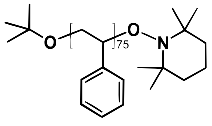


(4)

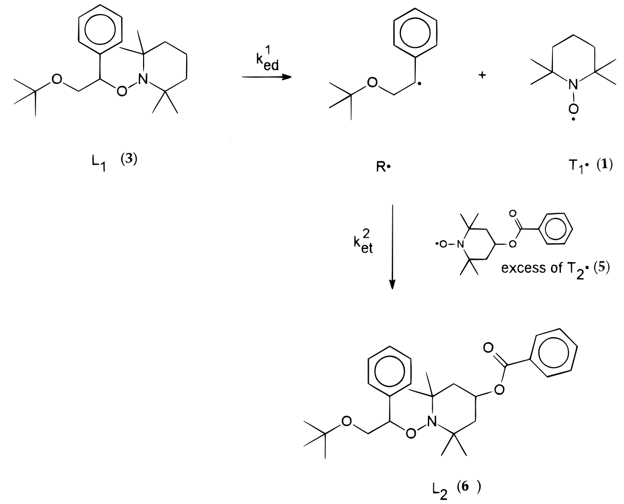
We will now show that quantitative ESR measurements, a tool to monitor the nitroxide production for an alkoxyamine species in solution in the presence of oxygen as scavanger, are an excellent and easy method to obtain accurate data for k_{ed}. Two alkoxyamine species, i.e., **3** and **4**, will be analyzed. The k_{ed} values obtained for **3** will be compared with the values obtained from nitroxide-exchange experiments. For the ease of the discussion these latter experiments will be treated first. The k_{ed} values for **4** will be compared with the values reported by Fukuda et al.[9] for the polymeric alkoxyamine **2**.

Alkoxyamine Homolysis in the Presence of a Different Nitroxide

A plausible option to study the homolysis is to exchange the nitroxide ($T_1^\bullet$) of the original dormant alkoxyamine (L_1) with a different nitroxide ($T_2^\bullet$) to yield a second alkoxyamine compound (L_2) (see Scheme 1).

The alkoxyamines indicated in Scheme 1, i.e., L_1 (**3**) and L_2 (**6**), were synthesized as model compounds to investigate the rate coefficient for homolytic dissociation (k_{ed}) of **3** over a range of temperatures in toluene. A typical nitroxide-exchange experiment comprised the monitoring of the concentrations of **3** and **6** from a thermostated 10^{-3} mol L^{-1} solution of **3** in the presence of 10^{-2} mol L^{-1} of nitroxide **5**. The concentrations of **3** and **6**, or molar ratios ($[L_2]/[L_1]$), vs time were followed by off-line HPLC.

Scheme 1. Pseudo-First-Order Nitroxide-Exchange System To Determine the Rate Coefficient for Alkoxyamine C−O Bond Cleavage (k_{ed}^1) of L_1



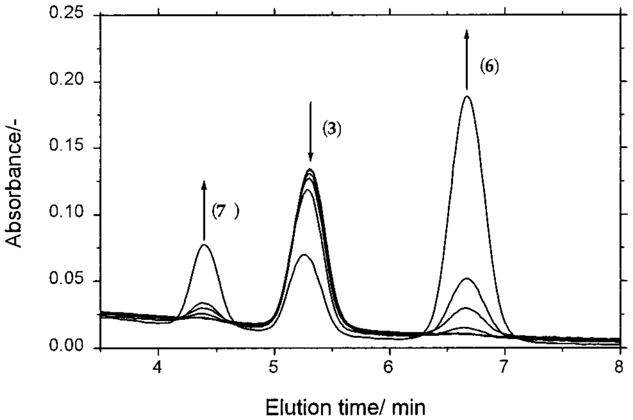


Figure 1. A typical set of HPLC chromatograms from the nitroxide-exchange experiment of **3** carried out in toluene at 363 K, as represented in Scheme 1. The data were recorded with a UV detector at 214 nm. Samples were taken from the system at 15, 30, 60, 120, 240, and 1330 min. Arrows indicate whether peaks increase or decrease in time. Numbers indicate compound assignment to peaks.

We will now shortly elucidate the kinetics involved to calculate values of k_{ed} from the acquired data. Next, our results on the determination of k_{ed} of alkoxyamine **3** in toluene using these nitroxide-exchange experiments will be presented.

Pseudo-First-Order Conditions. When the alkoxyamine C−O bond cleaves, a transient carbon-centered radical species is formed. This $R^\bullet$ can, in principle, undergo different events, such as bimolecular termination with a second $R^\bullet$, transfer to solvent, trapping via combination with $T_1^\bullet$ or $T_2^\bullet$, or trapping via disproportionation with $T_1^\bullet$ or $T_2^\bullet$.

A relatively high $[T_2^\bullet]$ ensures that the only fate of $R^\bullet$ is to be trapped with the different nitroxide $T_2^\bullet$. Under these conditions k_{ed} can be calculated from

$$\ln\left(\frac{[L_1]_t}{[L_1]_0}\right) = -k_{ed}^1 t \tag{1}$$

When we assume that trapping via disproportionation can be neglected, k_{ed} can be calculated from eq 2 (note: $[L_1]_{t=0} = [L_1]_t + [L_2]_t$).

$$\ln\left(1 + \frac{[L_2]_t}{[L_1]_t}\right) = k_{ed}^1 t \tag{2}$$

Results and Discussion

Nitroxide-exchange experiments were performed, following the general procedure outlined above, to investigate the k_{ed} of **3** in toluene at five different temperatures, i.e., 333, 343, 353, 363, and 373 K. A typical set of HPLC chromatograms recorded with a UV detector (214 nm) acquired from the experiment performed at 363 K is plotted in Figure 1.

The peaks observed at an elution time of 5.3 and 6.7 min are from **3** and **6**, respectively. A third peak, not expected initially, appeared with increasing intensity at an elution time of 4.4 min. HPLC analysis on a number of synthesized alkoxyamine compounds using a UV diode-array detector (200−600 nm) revealed that the unknown compound was alkoxyamine **7**.

Scheme 2. Hydrogen Atom Abstraction by a Nitroxide

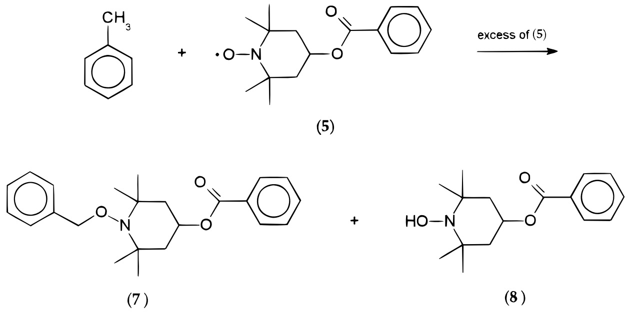


Table 1. k_{ed} Values of 3 in Toluene Determined with Nitroxide-Exchange Experiments

T/K	k_{ed}/s^{-1}	T/K	k_{ed}/s^{-1}
333	$1.6_0 \times 10^{-7}$	363	$1.0_5 \times 10^{-5}$
343	$6.7_3 \times 10^{-7}$	373	$3.3_8 \times 10^{-5}$
353	$2.7_0 \times 10^{-6}$		

This species can be formed via two different processes. The first is hydrogen atom transfer from toluene to the carbon-centered radical to yield 2-phenylethyl *tert*-butyl ether and a benzyl radical, which is trapped by **5** to yield alkoxyamine **7**. The second is a hydrogen atom abstraction from toluene by nitroxide **5** to yield a benzyl radical, which is subsequently trapped by a second molecule of nitroxide **5**, and the corresponding hydroxylamine **8** (see Scheme 2).[10]

No formation of 2-phenylethyl *tert*-butyl ether was detected in the nitroxide-exchange experiments performed with alkoxyamine **3**, which eliminates the first option. This can also be seen from k_{tr}^{Tol}[toluene]/k_{et}[(**5**)] $\ll 10^{-2}$, confirming that pseudo-first-order conditions are valid; i.e., the exclusive fate or R$^•$ is to be trapped with nitroxide **5**. The formation of alkoxyamine **7**, therefore, must have taken place via the second route, i.e., hydrogen atom abstraction from toluene by nitroxide **5**. The occurrence of this reaction was confirmed in an experiment where toluene was heated in the presence of nitroxide **5**.

This side reaction (see Scheme 2) caused an additional decrease in the concentration of nitroxide **5**, which turned out not to intervene the pseudo-first-order conditions, since **5** was present in a large amounts.

The acquired HPLC data (see Figure 1) were converted using calibration curves obtained from stock solutions of **3** and **6**. Investigation of both [L$_1$] vs time (see eq 1) and [L$_2$]/[L$_1$] vs time (see eq 2) as data sets for the determination of k_{ed} yielded identical values for k_{ed} within experimental error. This supports the assumption that trapping via disproportionation can be neglected. (Moreover, no products from R$^•$ as a result of transfer to solvent, bimolecular termination, or trapping via disproportionation were detected.)

The use of [L$_2$]/[L$_1$] vs time has the advantage that variation of the injection volume of the samples for HPLC analysis is ruled out. Consequently, the [L$_2$]/[L$_1$] vs time data sets were used to calculate values of k_{ed}, using a nonlinear-least-squares (NLLS) method assuming a relative estimated error structure. These final data sets are plotted in Figure 2a,b. The calculated values of k_{ed} obtained from these nitroxide-exchange experiments are summarized in Table 1.

From these rate coefficients the parameters for the Arrhenius equation were determined, again with a NLLS method assuming a relative estimated error structure.[11]

$$k_{ed} = 9.1_2 \times 10^{14} \exp\left(\frac{-138._8 \times 10^3}{RT}\right) \tag{3}$$

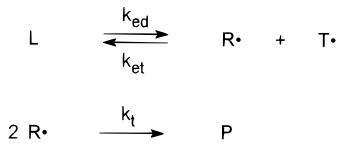
We have to check whether the assumed pseudo-first-order conditions were valid for these nitroxide-exchange experiments. The HPLC analysis showed no traces of products from bimolecular termination of R$^•$, transfer to solvent of R$^•$, and trapping via disproportionation.

A side reaction, however, that has to be considered is the trapping of R$^•$ with T$_1^•$. In that way, the original alkoxyamine is formed back, which leads to an underestimation of [L$_2$]/[L$_1$] and, thus, k_{ed}. When we take ln(1 + [L$_2$]/[L$_1$]) = 0.15 (all data acquired are below this value, see Figure 2a,b), we can calculate that ca. 14% of T$_1^•$ from alkoxyamine L$_1$ is exchanged for T$_2^•$. In our experiments $[L_1]_0 = 1.0 \times 10^{-3}$ mol L^{-1} and $[T_2^•]_0 = 1.0 \times 10^{-2}$ mol L^{-1}, so that now $[T_1^•] = 1.39 \times 10^{-3}$ mol L^{-1} and $[T_2^•] = 9.86 \times 10^{-3}$ mol L^{-1}. When we assume that $k_{et}^1 = k_{et}^2$ and neglect all other events than trapping via coupling, this leads to a value of 0.986 for the probability of R$^•$ to be trapped with T$_2^•$ via coupling. This implies that the pseudo-first-order conditions were valid.

Alkoxyamine Homolysis in the Presence of Oxygen

We initially considered online monitoring of [T$^•$] vs time from a properly degassed solution of an alkoxyamine, as a valuable method to obtain insight into the processes of homolytic dissociation, trapping via coupling, and bimolecular termination. The reactions that were accounted for are given in Scheme 3.

Scheme 3. Model System



When we consider this model system, the alkoxyamine (L) will dissociate in a radical species R$^•$ and the nitroxide T$^•$ at elevated temperatures. The radical R$^•$ can undergo either permanent bimolecular termination to yield a product P or trapping with T$^•$. The rate equations for T$^•$ and R$^•$ for this specific system are given by

$$\frac{d[T^•]}{dt} = k_{ed}[L] - k_{et}[R^•][T^•] \tag{4}$$

$$\frac{d[R^•]}{dt} = k_{ed}[L] - k_{et}[R^•][T^•] - 2k_t[R^•]^2 \tag{5}$$

Under these boundary conditions, i.e., $t = 0$ s, $[T^•] = 0$ mol L^{-1}, $[R^•] = 0$ mol L^{-1}, and $[L] = [L]_0$, eqs 4 and 5 reduce to respectively

$$\frac{d[T^•]}{dt}\Big|_{t=0} = k_{ed}[L]_0 \tag{6}$$

$$\frac{d[R^•]}{dt}\Big|_{t=0} = k_{ed}[L]_0 \tag{7}$$

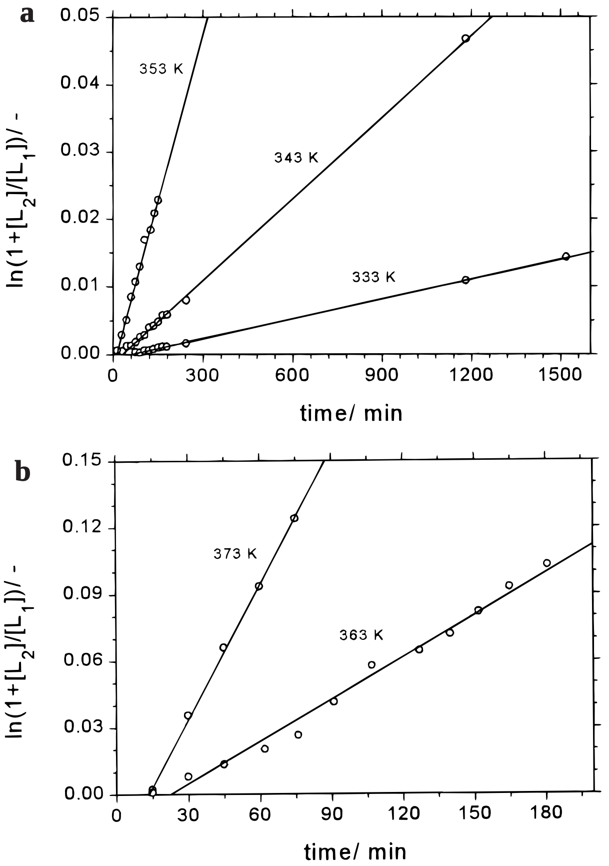


Figure 2. (a) Data obtained from the nitroxide-exchange experiments of **3** in toluene at 333, 343, and 353 K. The lines represent the fit according to eq 2. **(**b) Data obtained from the nitroxide-exchange experiments of **3** in toluene at 363 and 373 K. The lines represent the fit according to eq 2.

The initial slope of the monitored [T$^\bullet$] vs time data divided by the initial alkoxyamine concentration ([L]$_0$) leads to k_{ed}.

In Figure 3a,b, [T$^\bullet$] and [R$^\bullet$] vs time are plotted, together with the functions [T$^\bullet$] = k_{ed}[L]$_0$$t$ and [R$^\bullet$] = k_{ed}[L]$_0$$t$, for the model system represented by Scheme 3. The input parameters used in the simulations are given in the Experimental Section.

As can be observed in these plots, an accurate determination of k_{ed} from the [T$^\bullet$] vs time plot would require a data acquisition time scale of milliseconds. The time scale of a typical quantitative ESR measurement carried out in this study was, however, limited to minutes rather than milliseconds, due to experimental restrictions. Moreover, it is likely that the instantaneous isothermal conditions needed to obtain an accurate initial slope cannot be achieved experimentally. This curtails the possibility to obtain an accurate value of the alkoxyamine C−O bond homolysis (k_{ed}), and a solution needs to be found to prolong the time scale for which pseudo-first-order kinetics can be applied.

Results and Discussion

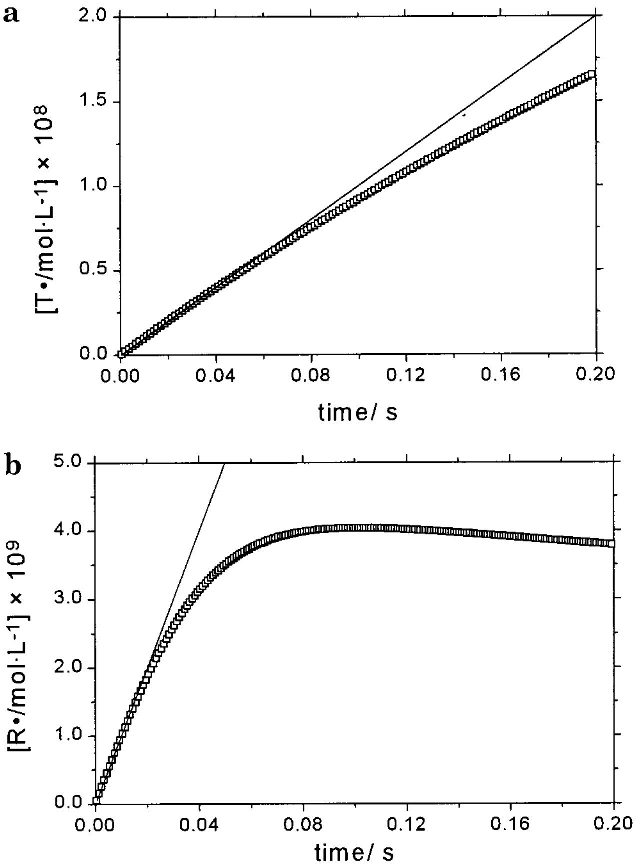


Figure 3. (a) Simulated [T$^\bullet$] vs time (□) and [T$^\bullet$] = k_{ed}[L]$_0$$t$ (—) for the model system represented by Scheme 3, using the input parameters listed in the Experimental Section. (b) Simulated [R$^\bullet$] vs time (□) and [R$^\bullet$] = k_{ed}[L]$_0$$t$ (—) for the model system represented by Scheme 3, using the input parameters listed in the Experimental Section.

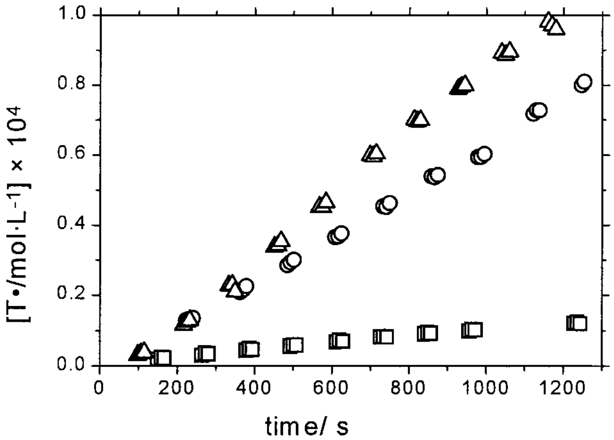


Figure 4. A 0.01 mol L^{-1} solution of **3** in toluene at various temperatures. [T$^\bullet$] vs time at 353 K (□), 363 K (○), and 373 K (△) measured with quantitative ESR. Prior to the experiment all samples were purged with argon to remove oxygen.

Inspired by the theoretical “ideal” system described above, ESR experiments were carried out with degassed 0.01 mol L^{-1} solutions of alkoxyamine **3** in toluene to monitor online the TEMPO **1** concentration at a specific temperature. In Figure 4 the results obtained at 353, 363, and 373 K are presented. It is important to mention that these samples were degassed by purging with argon.

As can be observed, the initial slopes of these samples appear to be linear over a time period exceeding 10^3 s. The apparent rate coefficients for the homolytic dissociation of **3** in toluene (k_{ed}^{app}) calculated from the initial slopes are given in Table 2.

The observed linearity and, consequently, the rate values obtained from these data are in sharp contrast with the results obtained from the model system.

Table 2. k_{ed}^{app} of 3 in Degassed Toluene Determined with Quantitative ESR Measurements

T/K	k_{ed}^{app}/s^{-1}
353	1.1×10^{-6}
363	6.2×10^{-6}
373	9.1×10^{-6}

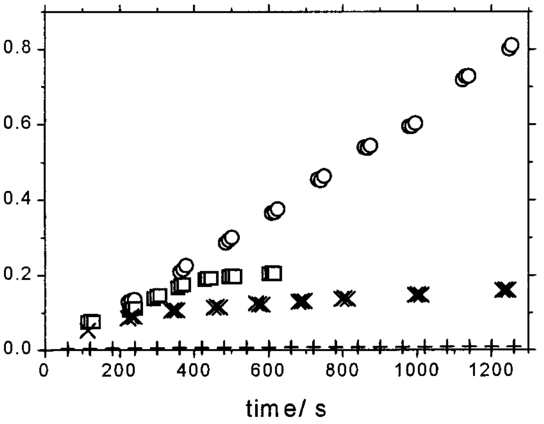


Figure 5. A 0.01 mol L^{-1} solution of **3** in toluene at 363 K. [T$^{•}$] vs time measured with quantitative ESR. Prior to analysis sample (O) was purged with argon, and samples (□) and (×) were purged with helium to remove oxygen. (+) represents the simulated [T$^{•}$] vs time for the model system represented by Scheme 3 using the input parameters listed in the Experimental Section.

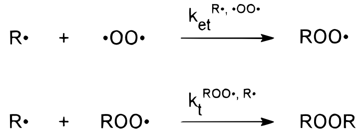
The experiments were therefore repeated with the "minor" difference that the samples were now degassed with helium instead of argon.[12] In Figure 5 the results obtained for the 0.01 mol L^{-1} solution of **3** in toluene at 363 K together with a simulation described by Scheme 3 are plotted.

As can be seen in this figure, different results were obtained in each case. Various experimental parameters and conditions, such as the stability of both the alkoxyamine (on storage) and the TEMPO **1** stock solutions and the used ESR parameters, were evaluated to account for the observed discrepancy. In the end, the remaining amount of oxygen in the samples was assigned as the cause for the variable results.

Trapping of a carbon-centered radical by oxygen yields a peroxide radical and competes with the trapping reaction with TEMPO. Since the majority of the nitroxide species are unable to trap oxygen-centered radicals,[13] this side reaction accounts for higher concentrations of TEMPO in comparison with systems characterized by complete absence of oxygen.

To illustrate this, simulations were performed on the basic model system given in Scheme 3, extended with the two dominant reaction events that may occur when oxygen is present in the system (see Scheme 4).[7,14]

Scheme 4



Since these simulations were performed to elucidate the effect on the concentration of nitroxide monitored vs time, the concentration of oxygen was kept at a constant value, i.e., [O$_2$] = 0, 1.0×10^{-8}, 1.0×10^{-6}, and 1.0×10^{-4} mol L^{-1}. The other input parameters are listed in the Experimental Section. The results are presented in Figure 6.

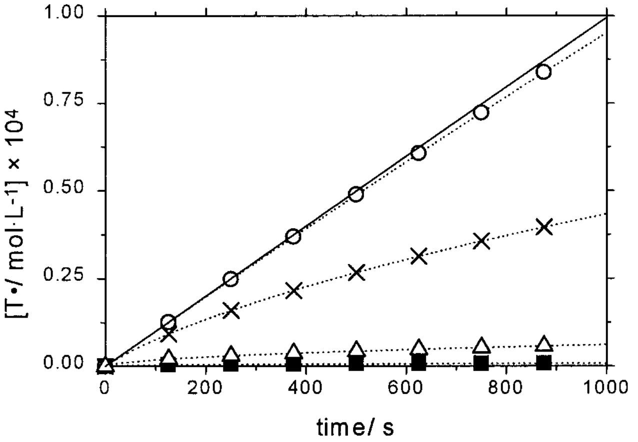


Figure 6. [T$^{•}$] vs time for the model system represented by Schemes 3 and 4 using the input parameters listed in the Experimental Section in the presence of various constant oxygen concentrations. (· · ·) is output from simulations. The points are included for clarity and for comparison with quantitative ESR data; (O) [O$_2$] = 1.0×10^{-4} mol L^{-1}; (×) [O$_2$] = 1.0×10^{-6} mol L^{-1}; (△) [O$_2$] = 1.0×10^{-8} mol L^{-1}; (■) [O$_2$] = 0 mol L^{-1}. (—) represents the function [T$^{•}$] = k_{ed}[L]$_0t$.

The results shown in Figure 6 demonstrate that a higher amount of oxygen indeed enhances the production of nitroxide. Another striking result is that the initial slope at high oxygen concentrations coincides with k_{ed}[L]$_0$ and, therefore, obeys pseudo-first-order kinetics.

The saturation concentration of oxygen in toluene under an atmosphere of pure oxygen is reported to be about 8.64×10^{-3} mol L^{-1}(at 293, 303, and 313 K).[15] Taking into account that the molar oxygen contents in air is approximately 20%,[16] a considerable amount of oxygen in nondegassed 0.01 mol L^{-1} samples of **3** in toluene will be present. This implies that for the initial stages of the quantitative ESR experiments using nondegassed samples, pseudo-first-order kinetics can be assumed.

On the basis of the above, we decided to perform our measurements under atmospheric conditions (i.e., without degassing the samples). A 0.01 mol L^{-1} solution of **3** in toluene was analyzed at 333, 343, 353, 363, and 373 K. The results of [T$^{•}$] vs time are plotted in Figure 7.

The values of k_{ed} were determined from these ESR data with eq 8, using a NLLS method:

$$\frac{[\mathrm{T}^{\bullet}]}{[\mathrm{L}]_0} = k_{ed}t + C \qquad (8)$$

where C is a constant to account for noninstantaneous conditions. The calculated k_{ed} values are summarized in Table 3.

From these values of k_{ed} at various temperatures, the parameters of the Arrhenius equation were determined (see eq 9), again with a NLLS method assuming a relative estimated error structure.[11]

$$k_{ed} = 1.1_0 \times 10^{14} \exp\left(\frac{-133._2 \times 10^3}{RT}\right) \qquad (9)$$

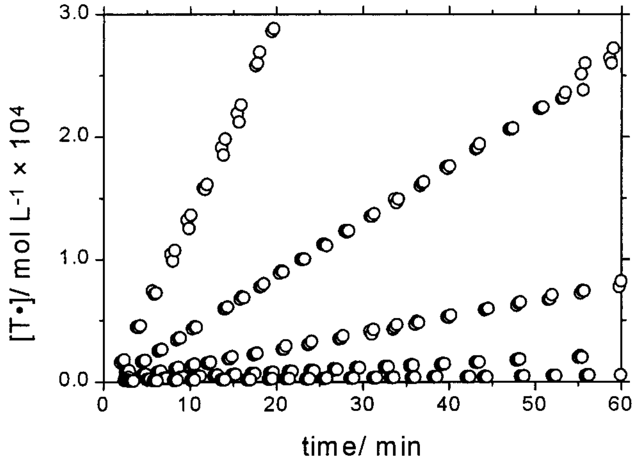


Figure 7. [TEMPO] vs time measured by quantitative ESR for a 0.01 mol L^{-1} solution of **3** in toluene at 333, 343, 353, 363, and 373 K. Note that the concentrations are based on the volume at room temperature.

Table 3. $\mathbf{k_{ed}}$ **Values of 3 and 4 in Toluene Determined with Quantitative ESR Measurements**

	k_{ed} /s^{-1}	
T/K	**3**	**4**
333	$1.4_5 \times 10^{-7}$	$8.6_7 \times 10^{-7}$
343	$6.0_2 \times 10^{-7}$	$3.2_9 \times 10^{-6}$
353	$2.2_3 \times 10^{-6}$	$1.6_2 \times 10^{-5}$
363	$7.4_7 \times 10^{-6}$	$6.0_5 \times 10^{-5}$
373	$2.5_8 \times 10^{-5}$	$1.8_3 \times 10^{-4}$

Similar quantitative ESR measurements were performed in toluene on the polymeric alkoxyamine (**4**: $\langle M_n \rangle = 7.6 \times 10^3$ g mol^{-1}, $\gamma = 1.26$, and $P_{dead} = 5\%$). The results for the k_{ed} values are also given in Table 3. The resulting Arrhenius equation is given by

$$k_{ed} = 1.0_2 \times 10^{16} \exp\left(\frac{-140._9 \times 10^3}{RT}\right) \qquad (10)$$

In Figure 8 the results of the k_{ed} values, and Arrhenius equations, of alkoxyamine **3** in toluene obtained from both the HPLC experiments, in which $R^•$ was scavenged by a different nitroxide species **5**, and the quantitative ESR measurements, in which $R^•$ was scavenged by molecular oxygen, are summarized. The apparent k_{ed} values obtained from degassed solutions of **3** via ESR measurements are also included. Moreover, the results for the polymeric alkoxyamine (**4**: $\langle M_n \rangle =$ 7.6×10^3 g mol^{-1}, $\gamma = 1.26$, and $P_{dead} = 5\%$) are given together with the Fukuda reported Arrhenius equation for **2**, with $\langle M_n \rangle = 1.7 \times 10^3$ g mol^{-1}, $\gamma = 1.11$, and P_{dead} = 5%: $A = 3.0 \times 10^{13}$ s^{-1} and $E_{act} = 124$ kJ mol^{-1}.

The two Arrhenius plots obtained for the alkoxyamine **3** are in reasonable agreement. The discrepancy between them, i.e., the higher values of k_{ed} obtained by the nitroxide-exchange experiments, pronouncing itself at higher temperatures, may have different causes. First, the ln(1 + $[L_2]/[L_1]$) vs time data obtained via HPLC analysis shows a larger deviation from its first-order fit than the data acquired with quantitative ESR measurements. This can most clearly be seen in Figure 2b for the HPLC data at 363 K. Second, the nitroxide-exchange experiments require relatively large amounts of nitroxide **5**, i.e., 1.0×10^{-2} mol L^{-1}. This nitroxide may influence the solvent characteristics of toluene or interact with other paramagnetic species, thereby changing their reactivity.

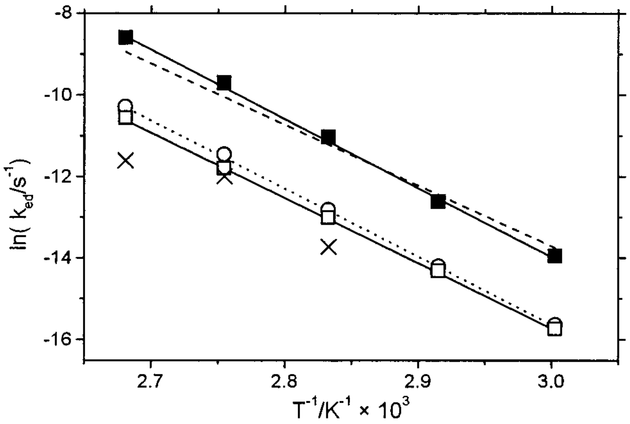


Figure 8. Linearized Arrhenius plot for k_{ed} values of **3** and **4** in toluene. Data for **3** from the nitroxide-exchange experiments (O, see also Table 1) and the calculated Arrhenius equation, with $E_{act} = 138._8 \times 10^3$ J mol^{-1} and $A = 9.1_2 \times 10^{14}$ s^{-1}, are given (· · ·, see also eq 3). Data for **3** and **4** from the quantitative ESR measurements (□ for **3** and ■ for **4**; see also Table 3) and the calculated Arrhenius equation, with $E_{act} = 133._2 \times 10^3$ J mol^{-1} and $A = 1.1_0 \times 10^{14}$ s^{-1} for **3** and $E_{act} = 140._9 \times 10^3$ J mol^{-1} and $A = 1.0_2 \times 10^{16}$ s^{-1} for **4**, are given (—, see also eqs 9 and 10). Moreover, k_{ed}^{app} values for **3** obtained from quantitative ESR measurements under argon (×, see also Table 1) and the Arrhenius equation for polystyrene alkoxyamine **2** reported by Fukuda, with $E_{act} = 124 \times 10^3$ J mol^{-1} and $A = 3.0 \times 10^{13}$ s^{-1} reported by Fukuda (- - -),[9] are included.

Both reasons favor the quantitative ESR measurement as a method to determine k_{ed}. Furthermore, when considered from an experimental point of view, the ESR method has the advantage that it only requires a sample of an alkoxyamine species and calibrated stock solutions of the nitroxide species. Elaborate conclusions on the accuracy of the data acquired with quantitative ESR measurements, however, can only be drawn from a larger data set for the k_{ed} of alkoxyamine **3**. This, however, is beyond the scope of this investigation.

Care must be taken with k_{ed} values determined from degassed ESR samples. Because of the restricted number of data points, the plot resulting from the acquired data can incorrectly be interpreted to be linear (see e.g. Figure 6). Hence, the determined values of the alkoxyamine homolysis (k_{ed}^{app}) will be underestimated for its true values (k_{ed}). This is clearly seen from our data obtained in degassed toluene samples in Figure 8.

It can be seen in Figure 8 that the data of Fukuda[9] and our work for the thermal homolysis of a polystyrene alkoxyamine are in good agreement. This confirms that both methods, i.e., alkoxyamine C−O bond cleavage in the presence of oxygen and monomer as scavenger, can be used to obtain correct kinetic data for k_{ed}. Furthermore, it can be observed that there is a chain-length dependence for the rate coefficient of alkoxyamine C−O bond homolysis, as the values for the polystyrene species are markedly higher than those of alkoxyamine **3**. This is mainly caused by the fact that upon homolysis the C−O bond stretching will result in an enhanced mobility of the nitroxide part of the molecule, which leads to a higher entropy of the system in the transition state. This effect will be most pronounced for the polymeric alkoxyamines. Hence, higher values for k_{ed} will be observed for these species primarily reflected in a higher preexponential factor. (A more detailed discussion on this will follow in a subsequent paper.) This is clearly seen in Figure 8.

Conclusions

In this paper it has been shown that monitoring the nitroxide concentration by quantitative ESR in the thermal homolysis of alkoxyamines in solution under atmospheric conditions is an easy and more important an accurate method to determine values for the rate coefficient for alkoxyamine C−O bond homolysis. This method can be applied to both alkoxyamines of low unimolecular weight and their polymeric analogues.

Experimental Section

Synthesis of Alkoxyamines. Di-*tert*-butyl peroxalate was synthesized using the procedure reported by Bartlett et al.[17] 4-Benzoyloxy-2,2,6,6-tetramethylpiperidin-*N*-oxyl (**5**) was synthesized from 4-hydroxy-2,2,6,6-tetramethylpiperidin-*N*-oxyl and benzoyl chloride. The latter was synthesized from 4-hydroxy-2,2,6,6-tetramethylpiperidine. Both were according to literature procedures.[18]

Alkoxyamine 3. TEMPO (**1**) (10 mmol, 1.56 g) and styrene (50 mL, 45 g) were mixed in a 100 mL round-bottomed flask. Di-*tert*-butyl peroxalate (5 mmol, 1.17 g) was added. The mixture was stirred until all compounds were completely dissolved and subsequently submitted to three freeze−pump−thaw cycles in order to remove the oxygen and to place the reaction mixture under an argon atmosphere. Next, the mixture was stirred and kept under argon for 3 days at 298 K. After this time period the excess of styrene was removed by vacuum distillation at room temperature. The crude alkoxyamine was purified by triple crystallization from methanol at 253 K. White crystals; yield 66%. ESR spectra of this compound in toluene showed no presence of free TEMPO ($[\mathrm{TEMPO}] < 10^{-8}$ mol L^{-1}).

^{1}H NMR ($\mathrm{CDCl_3}$): δ 1.04 (s, 9 H, $(\mathrm{C}H_3)_3\mathrm{CO}$), 0.58, 1.02, 1.19, 1.37 (br s, 3 H, $\mathrm{C}H_3$-ring), 0.9−1.7 (br m, 6 H, $\mathrm{C}H_2$-ring), 3.41 (dd, 1 H, H_a), 3.89 (dd, 1 H, H_b), 4.74 (dd, 1 H, H_c), 7.18−7.35 (m, 5 H, Ph).

^{13}C NMR gated-decoupled ($\mathrm{CDCl_3}$): δ 17.2 (t, 1 C, *C*(4)-ring), 20.3 (q, 2 C, $C\mathrm{H_3}$-ring), 27.3 (q, 3 C, $(C\mathrm{H_3})_3\mathrm{CO}$), 33.9 (q, 2 C, $C\mathrm{H_3}$-ring), 40.6 (t, 2 C, *C*(3)-ring and *C*(5)-ring), 60.0 (s, 1 C, *C*(2)-ring), 62.0 (s, 1 C, *C*(5)-ring), 65.0 (t, 1 C, $C\mathrm{H_aH_b}$), 72.8 (s, 1 C, $(\mathrm{CH_3})_3C\mathrm{O}$), 86.1 (d, 1 C, $C\mathrm{H_cPh}$), 127, 128, 129 (m, 5 C, $\mathrm{Ph_o}$, $\mathrm{Ph_m}$, $\mathrm{Ph_p}$), 142.5 (s, 1 C, Ph).

Alkoxyamine 6. This compound was synthesized using the above procedure for alkoxyamine **3**. TEMPO was replaced with 4-benzoyloxy-2,2,6,6-tetramethylpiperidin-*N*-oxyl. The crude alkoxyamine (two diastereomers; difference indicated with *) was purified by liquid chromatography over an aluminum oxide packing (activated neutral Brockmann I, STD grade, ca. 150 mesh, 58 Å; diethyl ether:petroleum ether 40−60; 25:75 v:v%). White solid; final yield 70%.

^{1}H NMR ($\mathrm{CDCl_3}$): δ 0.59 (br s, 3 H, $\mathrm{C}H_3$-ring), 1.09 (s, 9 H, $(\mathrm{C}H_3)_3\mathrm{CO}$), 1.16 (s, 9 H, $(\mathrm{C}H_3)_3\mathrm{CO}$)*, 1.17 (br s, 3 H, $\mathrm{C}H_3$-ring), 1.37 (s, 3 H, $\mathrm{C}H_3$-ring), 1.49 (s, 3 H, $\mathrm{C}H_3$-ring), 1.59 (dd, 2 H, $\mathrm{C}H_2$-ring), 1.74 (dd, 2 H, $\mathrm{C}H_2$-ring)*, 1.83−1.88 (dd, 2 H, $\mathrm{C}H_2$-ring), 1.97−2.00 (dd, 2 H, $\mathrm{C}H_2$-ring)*, 3.44 (dd, 1 H, H_a), 3.88 (dd, 1 H, H_b), 4.12 (dd, 1 H, H_a)*, 4.63 (dd, 1 H, H_b)*, 4.79 (dd, 1 H, H_c), 4.95 (dd, 1 H, H_c)*, 5.24 (dt, 1 H, $\mathrm{C}H\mathrm{O_2CPh}$), 7.15−8.01 (m, 10 H, Ph).

^{13}C NMR gated decoupled ($\mathrm{CDCl_3}$): δ 21.1 (q, 2 C, $C\mathrm{H_3}$-ring), 27.2 (q, 3 C, $(C\mathrm{H_3})_3\mathrm{CO}$), 33.8 (q, 2 C, $C\mathrm{H_3}$-ring), 44.8 (t, 2 C, *C*(3)-ring and *C*(5)-ring), 59.9 (s, 1 C, *C*(2)-ring), 61.0 (s, 1 C, *C*(5)-ring), 65.0 (t, 1 C, $C\mathrm{H_aH_b}$), 67.4 (d, 1 C, *C*(4)-ring), 72.9 (s, 1 C, $(\mathrm{CH_3})_3C\mathrm{O}$), 84.1 (d, 1 C, $C\mathrm{H_cPh}$), 86.4 (d, 1 C, $C\mathrm{H_c}$-Ph)*, 125.2−132.7 (m, 6 C, $\mathrm{Ph_o}$, $\mathrm{Ph_m}$, $\mathrm{Ph_p}$), 139.0 (s, 1 C, $\mathrm{CH_c}Ph$), 142.0 (s, 1 C, $Ph\mathrm{CO_2}$), 166.0 (s, 1 C, $C{=}\mathrm{O}$).

Alkoxyamine 7. This compound was synthesized using the above procedure for alkoxyamine **3**. Styrene was replaced with toluene. The crude alkoxyamine was purified by crystallization from petroleum ether. White crystals; yield 60%.

^{1}H NMR ($\mathrm{CDCl_3}$): δ 1.31, 1.33 (s, 6 H, $\mathrm{C}H_3$-ring), 1.76, 2.01 (dd, 2 H, $\mathrm{C}H_2$-ring), 4.85 (s, 2 H, $\mathrm{PhC}H_2$), 5.30 (dt, 1 H, $\mathrm{C}H\mathrm{O_2}$-CPh), 7.19−7.38 (m, 5 H, $Ph\mathrm{CH_2}$), 7.43 (dd, 2 H, $\mathrm{O{=}CPh_m}$), 7.55 (td, 1 H, $\mathrm{O{=}CPh_p}$), 8.02 (dd, 2 H, $\mathrm{O{=}CPh_o}$).

Polystyrene Alkoxyamine 4. This compound was obtained by a TEMPO-mediated living radical polymerization of styrene at 130 °C ($\langle M_\mathrm{n}\rangle = 7.6 \times 10^3$ g mol^{-1}, $\gamma = 1.27$; P_dead is ca. 5%). Prior to use styrene was distilled and passed over a column of inhibitor remover (Aldrich).

Styrene, alkoxyamine (**3**, 0.05 M), and a trace amount of TEMPO were charged into a three-necked 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stirrer. The reaction mixture was deaerated by three freeze−pump−thaw cycles in order to place the reaction mixture under an argon atmosphere. The flask was placed in a thermostated oil bath at the required temperature for a fixed period of time. The polymer was isolated by triple precipation from methanol.

Nitroxide-Exchange Reactions. The HPLC setup consisted of a Waters M6000 pump and a Waters 712WISP autoinjector. Injection volume was 12 μL for all experiments. A $\mathrm{C_{18}}$-modified silica column (Zorbax RX-C18, 4.6 × 150 mm, $d = 5$ mm) was used.

The eluent was 10% water (Super-Q, Waters) in 90% methanol (HPLC grade, BioSolve Ltd.), and the applied flow rate was 1 mL min^{-1}. The UV detector was a Waters 484 applied at 214 nm, and data acquisition and processing were performed with Waters Millennium (version 2.10) software. All measurements were carried out at 308 K. Calibration was carried out using stock solutions of compounds **3**, **6**, and **7**. The initial slopes representing the value of k_ed were obtained by a linear-least-squares method.

Procedure. Prior to use toluene were distilled and stored over molecular sieves (4 Å). Other solvents were of HPLC grade and used as purchased. Alkoxyamine **3** (5×10^{-5} mol, 0.0167 g) was dissolved in 50 mL of solvent together with a 10-fold excess of 4-benzoyloxy-2,2,6,6-tetramethylpiperidin-*N*-oxyl (**5**) (5×10^{-4} mol, 0.138 g). The mixture was degassed and placed under an argon atmosphere by three freeze−pump−thaw cycles. Reactions were carried out at various temperatures. Samples were taken every 10 min up to 3 h (immediately quenched with liquid nitrogen), and reactions were carried out up to 25 h or more. These samples were directly injected into the HPLC apparatus.

Quantitative ESR.[19] All measurements were carried out on a Bruker ER200D SRC spectrometer and/or a Bruker ESP 300E, operating with an X-band standard cavity (ν ca. 9.4 GHz) and interfaced to a Bruker Aspect 3000 data system. Temperature was controlled by a Bruker ER4111 variable temperature unit. The nitroxide concentrations were determined by double integration of the ESR spectra, and the data were calibrated with stock solutions of nitroxide measured in toluene under identical conditions.

ESR Parameters: center of field = 3345.00 G; sweep width = 100.00 G; modulation frequency = 100 kHz; modulation amplitude = 2.50 G; conversion time = 20.48 ms; time constant = 81.92 ms; resolution of field axis = 4096. A variable receiver gain was used, depending on the concentration of nitroxide in the sample.

Procedure. Prior to use toluene was distilled and stored over molecular sieves (4 Å). A 1×10^{-2} mol L^{-1} solution of the alkoxyamine in toluene was prepared. Approximately 1 mL was put in an NMR tube for analysis. (Some samples were deoxygenated by purging helium or argon through the solution in the NMR tube for several minutes.) Time-resolved measurements were performed at variable temperatures.

Simulations. The differential equations were solved using a Gear algorithm for solving a set of stiff differential equations, modified from the NAG library subroutine D02AEF. All calculations were performed on a Silicon Graphics Challenge XL Supercomputer.[20]

Input Parameters for Model System: $k_\mathrm{ed} = 1.0 \times 10^{-5}$ s^{-1}; $k_\mathrm{et} = 5.0 \times 10^8$ L mol^{-1} s^{-1}; $k_\mathrm{t} = 2.5 \times 10^9$ L mol^{-1} s^{-1}; $[\mathrm{L}]_0 = 1.0 \times 10^{-2}$mol L^{-1}; $[\mathrm{R}^\bullet]_0 = 0$ mol L^{-1}; $[\mathrm{T}^\bullet]_0 = 0$ mol L^{-1}.

Additional Input Parameters for Model System with Oxygen: $k_\mathrm{et}^{\mathrm{R}\bullet,\bullet\mathrm{OO}\bullet} = 5.0 \times 10^9$ L mol^{-1} s^{-1}; $k_\mathrm{t}^{\mathrm{ROO}\bullet,\mathrm{R}\bullet} = 3.0 \times 10^8$ L mol^{-1} s^{-1}.

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