Kinetics of Cap Separation in Nitroxide-Regulated “Living” Free Radical Polymerization: Application of a Novel Methodology Involving a Prefluorescent Nitroxide Switch

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Received March 1, 2001; Revised Manuscript Received June 7, 2001

ABSTRACT: A novel approach employing a prefluorescent paramagnetic sensor has been employed to determine the absolute kinetics for end-cap cleavage in TEMPO-capped polystyrene obtained by “living” free radical polymerization. This new methodology takes advantage of the suppression of coumarin fluorescence when this chromophore is tethered to a paramagnetic nitroxide. This coumarin−nitroxide is an excellent free radical trap for carbon-centered radicals; upon radical trapping, the resulting diamagnetic alkoxyamine is strongly fluorescent. Thus, fluorescence buildup is a direct measure of free radical formation and can be employed to quantify their formation or to study their kinetics. Studies of the temperature dependence of the process can be employed to determine activation parameters and bond dissociation energies. This simple technique can be employed to study the dynamics in the actual polymer systems, overcoming the frequent need to resort to model compounds.

Introduction

The methodology of “living” free radical polymerization (LFRP) offers the possibility of controlling polydispersity in free radical polymerization and the convenient design of block copolymers.[1−3] The “living” properties of LRFP derive from the reversible capping of the growing polymer chain with nitroxides. This cap readily dissociates at temperatures around 125 °C to allow further polymer growth.[2,4] The overall dynamics of LFRP is largely determined by the cap cleavage reaction and the small concentrations of nitroxide that accumulate in the system. Yet, determinations of the absolute kinetics of this key step have been difficult, and researchers have frequently resorted to small mimetic compounds that more easily overcome analytical problems and the inherent complexity of the polymeric system.

Nitroxides are persistent free radicals frequently used as radical scavengers or as quenchers of excited states. In particular, 2,2,6,6-tetramethylpiperidine-*N*-oxyl, known as TEMPO, has been used as a quencher of singlet and triplet excited states. Covalently tethering a nitroxide to a chromophore with a short link results in the intramolecular quenching of the chromophore’s excited state.[5] In the case of fluorescent moieties, the tethered nitroxide results in essentially quantitative suppression of the emission. Radical trapping leads to a diamagnetic alkoxyamine which acts as a switch, thus restoring the chromophore’s fluorescence. Blough and co-workers have shown that these covanlently linked nitroxide−fluorophore adducts can be employed as very sensitive optical sensors of radical/redox reactions.[5−8]

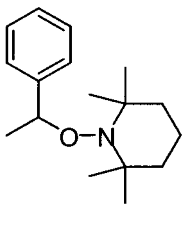
In this work, TEMPO has been covalently tethered via a short link, to a fluorescent chromophore (coumarin), leading to a nonflourescent paramagnetic compound ($CU-T^•$). When a TEMPO-capped polystyrene produced by LFRP is thermally decomposed in the presence of the sensor, the resulting macroradicals ($PS^•$) can be trapped by either TEMPO ($T^•$) or the prefluorescent probe ($CU-T^•$) with essentially the same kinetics. Thus, by adequately choosing the concentrations, it is possible to favor trapping by the probe, which results in a dramatic enhancement of the fluorescence (CU−T−PS) (Scheme 1).

This radical-switch methodology has been used for the first time in the determination of the dynamics of macroradicals derived from TEMPO-capped polystyrene using fluorescence spectroscopy. The rates of radical formation were determined; from these data we also obtained the kinetic Arrhenius parameters and the corresponding bond dissociation energy for the terminal TEMPO group in the polymeric chain.

Experimental Section

Synthesis of the Thermal Initiator: 2,2,6,6-Tetramethyl-1-(1-phenylethyoxy)-piperidine (EB−T). Typical conditions for the photochemical synthesis of the initiator were similar to those described in the literature.[10] One equivalent of nitroxide, TEMPO (Aldrich), was dissolved in 5 mass equivalents of di-*tert*-butyl peroxide (Aldrich), previously purified by passing it through a plug of neutral alumina (Aldrich). The red-orange solution was then diluted with 30−35 mL of ethylbenzene (99% purity, Aldrich) as solvent and reagent, loaded into a Pyrex test tube, and purged with nitrogen for 30 min. The solution was then irradiated with 300 nm broadband lamps until the color was discharged, typically 4−5 days. The lightly colored yellow solution so obtained was concentrated by bubbling a stream of nitrogen through the sample and then further concentrated under vacuum. Recrystallization from methanol afforded white crystals in greater than 90% yield.

EB-T



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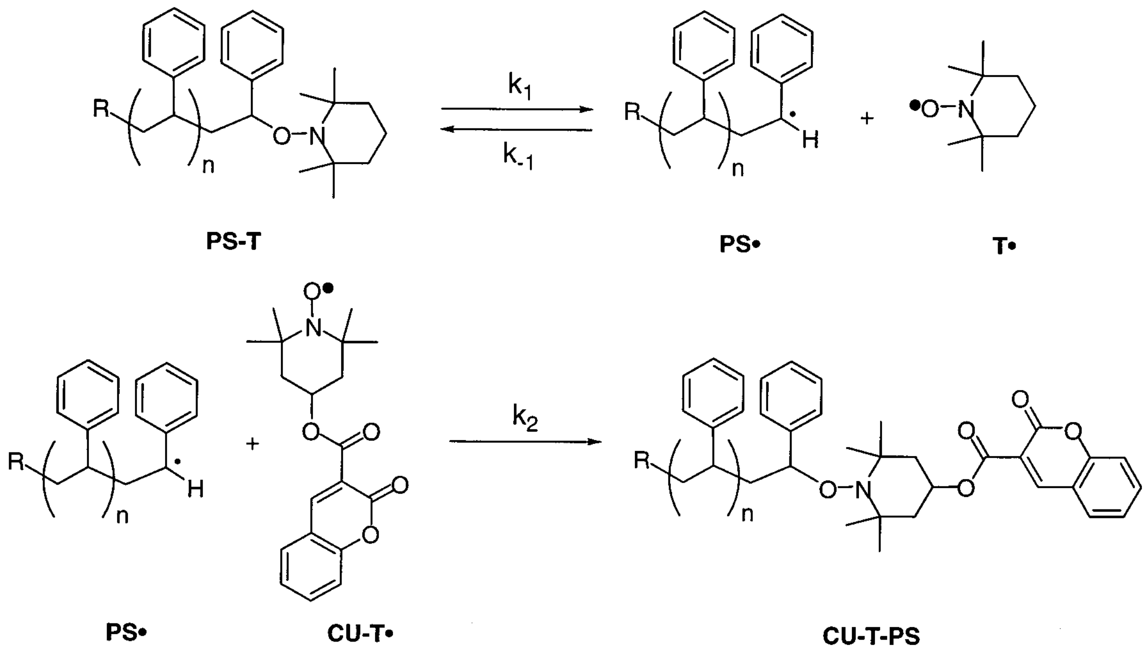
10.1021/ma0103831 CCC: $20.00 © 2001 American Chemical Society
Published on Web 07/31/2001

Scheme 1



Synthesis of the TEMPO−Coumarin Prefluorescent Probe (CU−T$^{\bullet}$). The TEMPO−coumarin sensor was synthesized by a procedure similar to that described by Hassner.[9] Coumarin-3-carboxylic acid (Aldrich) was esterified with 4-hydroxy-TEMPO in the presence of 1,3-dicyclohexanecarbodiimide and 4-(dimethylamino)pyridine in CH_2Cl_2 under argon for 2 h. After removal of the white precipitate 1,3-dicyclohexylurea the reaction mixture was washed three times with water and then concentrated. The residue was chromatographed over silica gel (hexane/ethyl acetate, gradient from 8:2 to 7:3) to obtain CU−T.

"Living" Free Radical Polymerization (LFRP) of Styrene (PS−T). The bulk polymerization reaction was carried out using freshly distilled styrene (Aldrich) as solvent. A 1:100 molar ratio of initiator (2,2,6,6-tetramethyl-1-(1-phenylethyoxy)piperidine) was dissolved in styrene and flame-sealed in 7 mm Pyrex glass tube after purging with nitrogen. The sample was then heated in a thermostated aluminum block at 125 ± 1 °C for 22 h.[10] After that, the sample was cooled, and any residual styrene was evaporated under vacuum; the resulting polymer was treated with methanol. A small amount of the resulting white precipitate was dissolved in THF and then analyzed by size exclusion chromatography (SEC) using Waters Styragel HR3 columns and a Varian refraction index detector. The molecular weight and polydispersity were determined relative to polystyrene molecular weight standards. A Jasco FP-1520 fluorescence detector was employed in some control experiments.

The average molecular weight (M_w) was 16 780, with a polydispersity of 1.23. This low polydispersity is typical of the LFRP method employed for the polymerization of styrene.[2,10,11]

Temperature Dependence. The thermal studies were carried out by adding an excess (1.5×10^{-4} M) of the prefluorescent probe to a chlorobenzene solution of polystyrene (1.5×10^{-6} M) prepared by LFRP and end-capped with TEMPO. The samples were purged with nitrogen for at least 30 min and sealed in a 1 × 1 cm quartz cell. The samples were then heated in a thermostated paraffin bath in a dark oven and were removed at selected time intervals. The reaction was stopped by cooling the reaction cell in an ice bath. The exterior of the sample cuvettes was cleaned with ethanol. The fluorescence spectra of the samples were then recorded using a PTI fluorimeter to quantify radical formation. The excitation wavelength was set to 350 nm to achieve selective excitation of the dye. Size exclusion chromatography with fluorescence detection demonstrated the incoporation of the chromophore on the polymer.

The rate constants were obtained by monitoring the growth of the fluorescence resulting from polymer radical trapping by the prefluorescent probe. Each point in the resulting Arrhenius plot represents the average of at least two measurements at each temperature according to eq 1, where I^{∞}, I^{0}, and I^{t} are the fluorescence intensities in the plateau, initially, and at time "t". The parameters k and t are the rate constant and the time.

$$\ln\left(\frac{I^{\infty} - I^{0}}{I^{\infty} - I^{t}}\right) = kt \tag{1}$$

When the reactions were carried out in absence of the TEMPO-capped polystyrene in control experiments, no changes in the fluorescence intensity were observed during the reaction time in the temperature range studied (90−135 °C), indicating that the probe is stable under these conditions. Thus, the increase of fluorescence observed occurs only when a carbon-centered radical is trapped by the prefluorescent probe, causing the fluorescence switch.

Results and Discussion

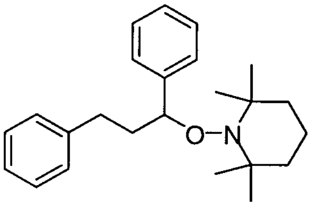
A coumarin−TEMPO paramagnetic adduct employed as a prefluorescent probe in the detection of polystyrene macroradicals is described here for the first time. A similar stategy was employed by Turro et al.[12] to prepare end-labeled monodisperse polymers. The time evolution of the fluorescence allows the determination of the rates of radical formation as well as its temperature dependence. From these data we calculate the kinetics and bond dissociation energy for the cleavage of the end nitroxide cap in polystyrene prepared by "living" free radical polymerization in the presence of TEMPO.

The general mechanism of nitroxide-regulated radical polymerization does not differ greatly from that of conventional free radical polymerization. The process can either be initiated by using typical initiators, such as benzoyl peroxide, or with unimolecular initiators derived from radical coupling with a nitroxide; the latter produce a stoichiometric mixture of nitroxide and an initiating radical. Both types of initiators polymerize by monomer addition, thus leading to a propagating radical. However, in the case of nitroxide-regulated polymerization, the propagating radical is trapped by the nitroxide forming an alkoxyamine. The new bond in PS–T (see Scheme 1) is relatively labile and is cleaved to regenerate two radicals ($R^\bullet$ and $N{-}O^\bullet$) at typical polymerization conditions around 125 °C.[4,13–16] The carbon-centered radical adds to the monomer repeatedly and is subsequently retrapped by nitroxide regenerating the "dormant" species. An equilibrium between the active and "dormant" species is established, in which the dormant species is favored.[16–20]

After polymerization at higher temperatures, the polymer at room temperature has its chain end capped with the nitroxide group in a stable alkoxyamine. Further exposure to heat can reinitiate the polymerization in the presence of the same or a different monomer; we have used this characteristic to remove the end TEMPO cap in the presence of an excess of the prefluorescent probe ($CU{-}T^\bullet$). Thus, the carbon-centered polystyrene radical adds to the coumarin–TEMPO probe and forms a highly fluorescence species (CU–T–PS) that can be optically detected (Scheme 1). We note that while both processes are reversible, the presence of an excess probe causes reaction 1 to be effectively irreversible, while any reversibility in reaction 2 is unimportant since the inescapable fate of $PS^\bullet$ radicals is the trapping by $CU{-}T^\bullet$. Once this criterion is met, the absolute concentration of $CU{-}T^\bullet$ does not enter in the calculations.

A number of initiators mimicking the chain end have been reported by us[4,10,21,22] and by others.[23,24] Use of model data to interpret polymer properties assumes that the C–O bond dissociation energy at the capped polymer end will be similar to those in other benzylic systems, such as the alkoxyamine derived from ethylbenzene (EB–T). The method used by us in our earlier reports was based on product analysis by HPLC following the thermal decomposition of various alkoxyamines in the presence of nitroxides. These alkoxyamine initiators were assumed to mimic well the reaction kinetics and thermodynamics for the LFRP process of styrene because they produce a similar radical to the propagating polymer radical in the polymerization of styrene. A number of estimates of this bond dissociation energy have been reported for these and related structures, ranging from 19 to 36 kcal/mol.[4,21,24–26] The compound EB–T is a good mimic for PS–T and leads to an estimated bond dissociation energy of 28.4 kcal/mol.[4] Similarly, for a compound containing two monomer units (PN–T) the value is 28.0 kcal/mol.[21]

PN-T



While other authors have either measured or estimated some of these kinetic parameters using similar mimetic compounds, this is the first study on the native polymeric system which takes advantage of such a simple, direct method. Our work has been performed under experimental condictions that allow the quantification of the carbon-centered radicals using an excess of CU–T.

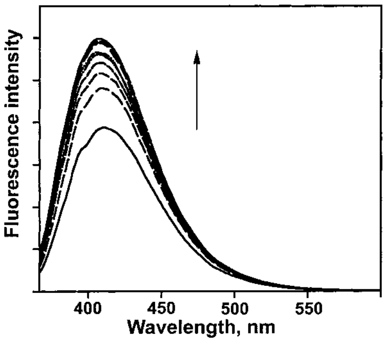


Figure 1. Dependence of the emission spectra of cumarine–TEMPO (1.5×10^{-4} M) in a chlorobenzene solution of polystyrene (1.5×10^{-6} M) with time at 125 °C. Data recorded at room temperature.

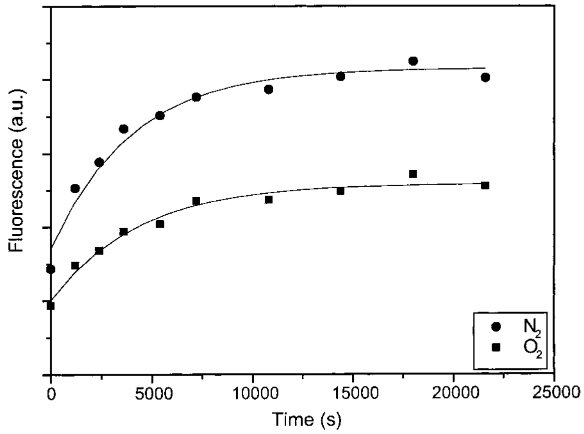


Figure 2. Determination of the rate constant for the trapping of the carbon-centered radicals of styrene with a prefluorescent probe (coumarin–TEMPO) by fluorescence. Measurements at 120 °C in chlorobenzene.

The reactions were studied between 90 and 135 °C in chlorobenzene as solvent. This solvent proved to be very convenient, allowing a suitable temperature range. Other solvents previously tested (acetonitrile, ethylbenzene) had inadequate temperature ranges or proved reactive toward the nitroxide at 125 °C. In a recent study of radical formation under laser excitation, benzene was employed as a solvent in the measurements of radical yields from photodecomposition of azobis(isobutyronitrile).[27]

When the reaction takes place in a thermostated bath, it is possible to establish a competition between TEMPO and coumarin–TEMPO adduct ($CU{-}T^\bullet$) for the trapping of the macroradicals of polystyrene in chlorobenzene. Thus, every trapping event of a carbon-centered radical causes the switch of a sensor to its highly fluorescent form (CU–T–PS), as illustrated in Figure 1. We note that some initial fluorescence is frequently observed and reflects the presence of small levels of diamagnetic impurities. This emission is not a problem, since measurements are normally based on the *difference*, i.e., the enhancement of fluorescence upon radical trapping, and the absolute concentration of $CU{-}T^\bullet$ is not required in the calculations. If anything, this characteristic makes for a rather robust method.

The individual rate constants were obtained from plots of product formation (i.e., fluorescence intensity) as a function of time, as illustrated in Figure 2 at 120 °C. It is important to note that at all temperatures the fluorescent product formation exhibited the same kinetic behavior, consisting of a rapid fluorescence increase in

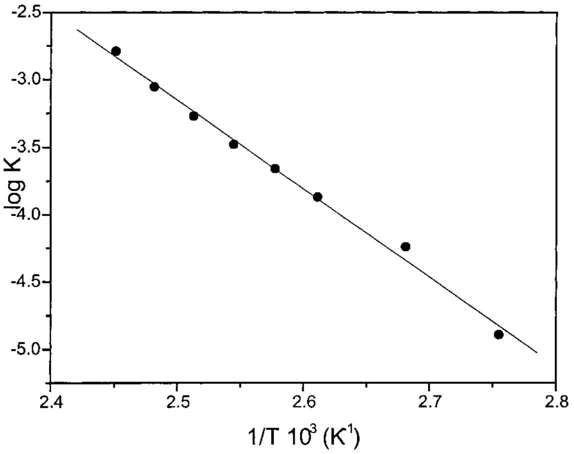


Figure 3. Arrhenius plot for the determination of the activation parameters for C−O bond cleavage in the TEMPO-capped polystyrene chain synthesized by the LFRP process.

the first stages of the reaction until a plateau is reached. An exception occurred at the lowest temperature studied (90 °C), at which the rate of product formation did not reach a plateau in the time examined. Measurements at various temperatures show that the rate of fluorescence increase decreases as the temperature of the medium decreases, as expected.

When these experiments were carried out under air, the fluorescence intensity increase was slower than in the experiments carried out under nitrogen (see Figure 2) and the plateau lower. It is well-known that molecular oxygen is able to inhibit radical-induced polymerization because of its high reactivity toward carbon-centered free radicals. Thus, these results support the mechanism proposed for the interaction between the radicals and the prefluorescent sensor. We note that with the diamagnetic analogues (e.g., coumarin) oxygen quenching only reduces the fluorescence intensity by 10 ± 3%; i.e., fluorescence quenching is minor relative to the changes shown in Figure 2.

From the experimental rate constants obtained at a series of temperatures, it is possible to determine the activation parameters for cap separation and from them to estimate the desired C−O bond dissociation energy. The Arrhenius plot (Figure 3) yields a preexponential factor ($\log A/\mathrm{s}^{-1} = 13.3$) related to the structure of the transition state and an activation energy ($E_a = 30.2$ kcal/mol) required for C−O bond cleavage. This compares with a reported activation energy of 30.3 kcal/mol for PN−T.[21] Using the estimated value of 2.3 kcal/mol for the activation energy for radical trapping,[28] the bond dissociation energy in PS−T can be estimated to be 27.9 kcal/mol.

The value of the preexponential factor measured is of the same order of magnitude as for model compounds PN−T and EB−T[4,21] and is consistent with homolytic bond cleavage processes for similar reactions. The transition states for the thermal decomposition of this system must lay close to the products, as implied by the relatively high preexponential factor. Also, a transition state with many degrees of freedom and a high entropy gain is implied by the large preexponential value.

In conclusion, this study was performed under typical LFRP conditions, and the similarity of the results obtained with the alkoxyamines that mimic the penultimate unit of styrene in a "living" free radical polymerization[21] validates our method for measuring the rate constants using prefluorescence probes for the optical detection of the radicals. The results agree well with those reported previously using unimolecular initiators[4,21] under nitroxide exchange conditions, and it is representative of the kinetics and thermodynamics occurring during the LFRP process. Beyond the applications reported by Blough[5−9] and by us here, prefluorescent nitroxide switches may find numerous other applications in areas of research involving "counting" free radicals,[27] polymer end-labeling,[12] or studying free radical kinetics.

Acknowledgment. The authors thank the Comunidad Autónoma de Madrid (C.A.M.) of Spain for the financial support through a postgraduate grant to O.G.B. J.C.S. thanks the Natural Sciences and Engineering Research Council of Canada for research and equipment grants.

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MA0103831