

Radical-Induced Oxidation of RAFT Agents—A Kinetic Study

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ABSTRACT: Radical-induced oxidation of reversible addition-fragmentation chain transfer (RAFT) agents is investigated with respect to the effect of molecular structure on oxidation rate. The radicals are generated by homolysis of either azobisisobutyronitrile or alkoxyamine and transformed *in situ* immediately into peroxy radicals through transfer to molecular oxygen. It is found that the oxidation rate depends on the structure of Z- and R-group of thiocarbonylthio compounds. For dithioesters with identical Z-phenyl substituent, the oxidation rate decreases in the order of cyanoisopropyl ($-\text{C}(\text{Me})_2\text{CN}$) > cumyl ($-\text{C}(\text{Me})_2\text{Ph}$) > phenylethyl ($-\text{CH}(\text{Me})\text{Ph}$) > 2-methoxy-1-methyl-2-oxoethyl ($-\text{CH}(\text{Me})-\text{C}(=\text{O})\text{OCH}_3$) > benzyl ($-\text{CH}_2\text{Ph}$).

For dithioesters with identical R-group, the oxidation rate decreases in the order of Z = phenyl- \sim benzyl- > RS- (trithiocarbonates) > RO- (xanthates). The stability of the RAFT agents toward oxidation correlates well with the chain transfer abilities as those previously reported by Rizzardo and co-workers. The priority of the oxidation reaction over the RAFT process, and the subsequent influence on RAFT polymerization are also investigated. © 2011 Wiley Periodicals, Inc. *J Polym Sci Part A: Polym Chem* 49: 1351–1360, 2011

KEYWORDS: kinetics; molecular structure; oxidation; RAFT; radical polymerization

INTRODUCTION Thiocarbonylthio compounds are widely used mediating agents in controlled/"living" radical polymerization based on reversible addition-fragmentation chain transfer (RAFT) process.^{1,2} The thiocarbonylthio moieties retain at the chain end of the polymerization product. The stability of the thiocarbonylthio compounds has attracted much attention, because it relates not only to the chain end functionality but also to the possible chain degradation of the polymerization product.^{3,4} The fidelity of thiocarbonylthio moieties at the chain ends has been proven by NMR^{5,7} and MALDI-TOF or ESI-MS.^{8–17} These functionalities can be removed deliberately by aminolysis,^{18–27} hydrolysis,^{28,29} and reduction,^{30–32} aiming to improve the degradation stability of the product or obtain a mercapto end group. Systematic studies^{19,33–40} using thermogravimetric analysis (TGA) have revealed that dithioesters undergo thermal decomposition at carbon-sulfur single bond, which is then used to completely remove thiocarbonylthio terminus of RAFT polymerization products.^{19,37–40} Thermal decomposition may also occur during polymerization, although to a much less extent, causing retardation and broadened molecular weight distribution.³⁴ The removal of thiocarbonylthio terminus for stabilization purpose is also achieved by post-treatment of polymer products with tributylstannane,⁴⁰ azobisisobutyronitrile (AIBN)^{41–43} or by ultraviolet radiation,^{44,45} which involves radical disproportionation process that form saturated or unsaturated chain ends.^{42,46}

In the background of organic chemistry, it has been reported that thiocarbonyl group can be converted into carbonyl group by a number of oxidizing agents, such as inorganic and organic peroxides, as well as molecular oxygen under irradiation.⁴⁷ Recently, Vana and coworkers performed oxidation reaction of the dithioester end group of poly(methyl methacrylate) (PMMA) using *tert*-butyl hydroperoxide.⁸ Zard and coworkers⁴⁸ achieved high yielding carbonyl group from thiocarbonyl group in xanthates by ozonolysis. Barner-Kowollik and coworkers⁴⁹ used the oxidation reaction induced by AIBN-derived radical in air in the presence of THF to prepare hydroxyl end-functionalized polymer. These findings pave a new way to functionalize RAFT polymer product.

It is important to note that AIBN-induced oxidation of thiocarbonylthio may relates to many reaction processes in RAFT-based polymerization. Trace amount of oxygen due to incomplete deaeration may lead to partial oxidation of the RAFT agent. This could be one of the reasons for the observation of thioester species in mass spectrometry,^{10–13,15,16,50–52} although peroxides in solvent tetrahydrofuran (THF) used for mass spectroscopy may also results in formation of thioester. AIBN treatment of RAFT polymerization product to remove thiocarbonylthio termini⁴¹ may also result in thioester moieties that retain at the chain ends. The preparation of dithioesters possessing leaving group derived from AIBN, for instance 2-cyanoprop-2-yl dithiobenzoate (CyDB), by the

Additional Supporting Information may be found in the online version of this article. Correspondence to: J. He (E-mail: jphe@fudan.edu.cn)
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RAFT process⁵³ may form oxidized byproduct in the presence of oxygen.

It is thus necessary to investigate the oxidation kinetics and affecting factors to achieve better control on the RAFT-based polymerization. The relationship between stability and molecular structure will be helpful for the development of "more oxygen tolerant" RAFT agents. The basic knowledge of the oxidation is also vital to the kinetic study of the RAFT process initiated by alkoxyamine, a model reaction developed in our laboratory.⁵⁴ In the present work, a series of thiocarbonylthio compounds with different leaving and activating groups are subject to radical induced oxidation. The dependence of oxidation rate on molecular structure, as well as the influence of the oxidation on RAFT polymerization, will be discussed.

EXPERIMENTAL

Materials

AIBN (Shanghai 4th Factory of Chemicals, 99%) was recrystallized from methanol. Methanol (Lingfeng Chemicals, 99.5%), petroleum ether (60–90 °C range, Shenxiang Chemicals, 99%), and dichloromethane (Lingfeng Chemicals, 99%) were dried over CaCl₂ and distilled before use. Cyclohexane (Feida, 99.5%), benzene (Shenxiang Chemicals, 99%) and toluene (Lingfeng Chemicals, 99%) was dried over sodium and distilled before use. Methyl methacrylate (MMA, Shanghai Fourth Factory of chemicals, 98%) and styrene (Yonghua Special Chemicals, 99%) were distilled after being stirred over CaH₂ for 24 h.

Measurements

High-performance liquid chromatography (HPLC) was performed on an instrument composed of a Waters 515 pump, a C-18 column and a UV detector with the wavelength set at 254 and 300 nm. Acetonitrile/water (v/v = 85/15) mixture was used as eluent (1.0 mL/min) at 40 °C. ¹H NMR and ¹³C NMR were carried out on a Bruker (500 MHz) NMR instrument, using tetramethylsilane (TMS) as the reference. Gel permeation chromatography (GPC) was performed on a Waters 410 system equipped with a guard column and three TSK columns (TSK Gel H-type, pore size 15, 30, and 200 Å) in series, a Waters 410 RI detector, using THF as the eluent at a flow rate of 1 mL/min at 40 °C. The columns were calibrated by narrow polystyrene standard with molecular weight ranging from 2.2 × 10³ to 5.2 × 10⁵ g/mol. Gas chromatography–mass spectrometry (GC-MS) was performed on an Agilent Technologies 6890N system, equipped with a mass-selective detector using electron impact ionization. Analytes were separated by a HP-5MS capillary column of 30 m (0.25 i.d. and 0.25-μm film thickness), which was inserted directly into the ion source of the MS system. Helium (99.999%) was the carrier gas maintained at a flow-rate of 1.0 mL/min. The injector was kept at 280 °C, and samples were split injected (1 μL, split ratio 100:1). The column oven temperature was programmed to start at 80 °C for 2 min, ramp at 10 °C/min to 280 °C, and held at 280 °C for 5 min. EI spectra were scanned between 50 and 550 Da in the full-scan acquisition mode. The transfer line and EI source tem-

perature were both 230 °C. The electron multiplier voltage was set on 70 eV.

Matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF MS) analysis were performed on a Voyager-DE STR (Applied Biosystems, Framingham, MA) equipped with a nitrogen laser emitting at 337 nm with a 3-ns pulse duration. The instrument was calibrated with Angiotensin and Insulin and operated in the reflector mode. The accelerating potential is 20 kV. For each spectrum, 1000 laser shots were accumulated. The matrix used was *R*-cyano-4-hydroxycinnamic acid (CHCA). Samples were prepared by mixing the solution of polymer (5 μL, 10 mg/mL in CHCl₃), the matrix (45 μL, 10 mg/mL in methanol) and sodium trifluoroacetate (STFA, cationizing agent, 5 μL, 10 mg/mL in methanol). An aliquot of 1 μL of the resulting mixture was spotted on the gold plate and air-dried.

Syntheses of the RAFT Agents

All RAFT agents were synthesized according to literature.^{53,56–58} The characterization results of ¹H NMR, FTIR, and GC-MS are given in Supporting Information.

Oxidation Reaction of RAFT Agents

Thiocarbonylthio compounds (as listed in Table 1; 0.1 mmol) and AIBN (0.032 g, 0.2 mmol) were dissolved in benzene (10 mL) in a 100-mL flask, which was then sealed without degassing. The reaction mixture was heated at 60 °C for a predetermined period.

Oxidation Reaction of PEDB in the Presence of Alkoxyamine

1-Phenylethyl dithiobenzoate (PEDB; 0.026 g, 0.1 mmol) and 1-(2,2,6,6-tetramethylpiperidinyloxy)-1-phenyl-ethane (PEET; synthesized according to literature procedures⁵⁵; 0.065 g, 0.4 mmol) were dissolved in cyclohexane (10 mL) in a 100-mL flask, which was then sealed without degassing. The reaction mixture was heated at 90 °C for a period of 16 h.

Oxidation Reactions of Polymeric RAFT Agents, PMMA-RAFT, and PS-RAFT

PMMA-RAFT (0.280 g, 0.1 mmol) and AIBN (0.065 g, 0.4 mmol) were dissolved in benzene (10 mL) in a 100-mL flask, which was then sealed without degassing. The reaction mixture was heated at 60 °C for 4 h before quenched into liquid nitrogen to stop the reaction.

PS-RAFT (0.228 g, 0.1 mmol) reacts with AIBN under the same conditions as in PMMA-RAFT system.

RESULTS AND DISCUSSION

The Oxidation of Thiocarbonylthio Compounds Initiated by AIBN

The oxidation reactions are performed by heating the solution of RAFT agents, either small molecular or polymeric, in the presence of air and AIBN. The results are listed in Table 1. As an example, PEDB, which is stable in air up to 100 °C in the absence of AIBN (run 1 in Table 1), is completely oxidized at 60 °C within 8 h in the presence of both air and AIBN. The oxidation reaction is monitored by ultraviolet–visible spectroscopy (UV–vis) and high-performance liquid

TABLE 1 Experimental Conditions and Results of Oxidation Reaction

| Run | Dithioester ^a | Radical Source | Feed Molar Ratio | Atmosphere | Temperature (°C) | Reaction Time (h) | Solvent | Product |
|-----|--------------------------|----------------|------------------|----------------|------------------|-------------------|----------------------------|----------------|
| 1 | | – | – | air | 100 | 16 | <i>tert</i> -butyl benzene | no reaction |
| 2 | | AIBN | 1:10 | N ₂ | 80 | 4 | Benzene | |
| 3 | | AIBN | 1:2 | air | 60 | 8 | Benzene | |
| 4 | | AIBN | 1:2 | Air | 60 | 8 | Benzene | |
| 5 | | AIBN | 1:2 | Air | 60 | 8 | Benzene | |
| 6 | | AIBN | 1:2 | Air | 60 | 4 | Benzene | |
| 7 | | AIBN | 1:2 | Air | 60 | 3 | Benzene | |
| 8 | | AIBN | 1:2 | Air | 60 | 10 | Benzene | |
| 9 | | AIBN | 1:2 | Air | 60 | 38 | Benzene | |
| 10 | | AIBN | 1:2 | Air | 60 | 46 | Benzene | |
| 11 | | AIBN | 1:2 | O ₂ | 60 | 5 | Benzene | |
| 12 | | PEET | 1:4 | Air | 90 | 16 | Cyclohexane | |
| 13 | | PEET | 1:4 | N ₂ | 90 | 8 | Cyclohexane | |
| 14 | PS-RAFT ^b | AIBN | 1:4 | Air | 60 | 4 | Benzene | PS-thioester |
| 15 | PMMA-RAFT ^b | AIBN | 1:4 | Air | 60 | 4 | Benzene | PMMA-thioester |

^a PEDB, CDB, BDB, CyDB were synthesized according to literature ref. 53. BDES was synthesized according to literature ref. 56. DBTTC was synthesized according to literature ref. 57. EtoCDB was synthesized according to literature ref. 58.

^b PS-RAFT and PMMA-RAFT are polystyrene ($M_{n,GPC} = 2280$ g/mol, $M_w/M_n = 1.10$) and poly(methyl methacrylate) ($M_{n,GPC} = 2800$ g/mol, $M_w/M_n = 1.14$), respectively, prepared by RAFT polymerizations mediated by cumyl dithiobenzoate (CDB).

chromatography (HPLC). As shown in Figure 1, the absorption band at 300 nm of dithioester decreases along with time and finally disappears at 8 h. The solution changes from pink to light yellow in color (inset in Fig. 1). This corresponds to a decrease in PEDB peak and an increase in a new peak at retention time = 6.4 min in HPLC diagram. ¹H NMR spectrum in Figure 2 shows all aromatic, methyl and methine protons, whose chemical shifts and integration values correlates to the expected oxidized structure. More importantly, the structure of thioester in the oxidation product is confirmed by the presence of signals at $\delta = 191$ ppm

in ¹³C NMR spectrum [Fig. 2(b)], which is assigned to carbonyl group (The signal for thiocarbonyl group should be at ~ 234 ppm⁵⁹). Figure 3 shows the gas chromatography-mass spectroscopy (GC-MS) results, in which the molecular ion at $m/z = 242$ is assignable to the anticipated oxidation product, 1-phenylethyl benzothioate (PEBT), while the base peak is benzoyl cation ($m/z = 105$).

All of the RAFT agents in Table 1 undergo oxidation in a way in which carbonyl sulfur is replaced by oxygen. This desulfurization of thiocarbonyl moiety in dithioesters has long

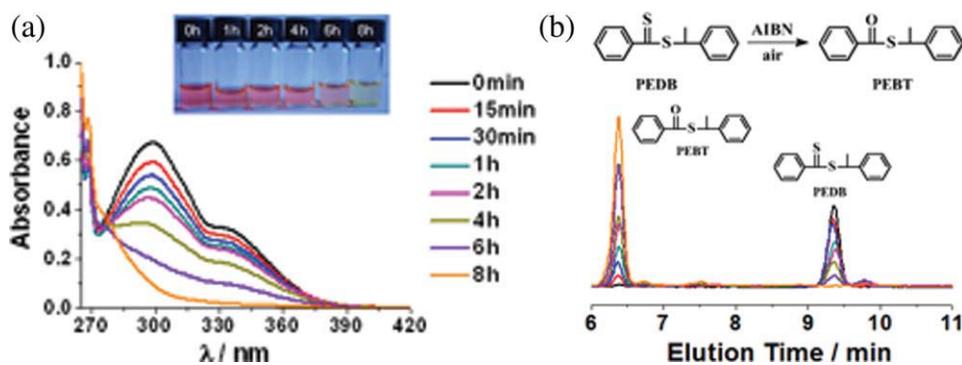


FIGURE 1 UV-vis spectrometry (a) and HPLC (b) monitoring the oxidation reaction of PEDB (0.026 g, 0.1 mmol) and AIBN (0.032 g, 0.2 mmol) in benzene at 60 °C in the presence of air. The insets are snapshots of the reaction vessels showing the color change during the reaction.

been achieved using oxidation reagents such as $\text{Hg}(\text{CH}_3\text{COO})_2$, KMnO_4 , and meta-chloroperoxybenzoic acid.⁶⁰ Nevertheless, the study on radical induced oxidation, as that in the present case, in the RAFT system is still scarce.^{8,49} It is also noted that azo-type radical initiator such as AIBN are widely used to create the peroxy radical oxidation environment in organic and pharmaceutical chemistry.⁶¹ The same species, that is, the peroxy radical, is supposed to be the oxidizing agent in the present work. Thus, the peroxy radical adds to thiocarbonylthio moiety to form an intermediate radical, which cyclizes into oxathiirane⁶² and expels a cyanoisopropoxy radical. The oxathiirane transforms into more stable carbonyl moiety and releases sulfur.⁶² Indeed, yellowish solid was observed on the wall of the flask during oxidation reaction. One of the possible further pathway of the expelled cyanoisopropoxy radical is to react with thiocarbonylthio moiety again, forming another carbonyl species through the oxathiirane intermediate, and expel a cyanoisopropyl radical. The overall oxidation reaction process is tentatively proposed in Scheme 1.

Influence of Molecular Structure on Oxidizability of Thiocarbonylthio Compounds

The oxidation rate of dithioester is a function of concentrations of dithioester and peroxy species. Thus, the conversion rate exhibits a decaying mode along with reaction time due to consumption of AIBN and oxygen. Nonetheless, dithioesters are readily oxidized to 100% conversion, provided that the peroxy species is enough. The oxidizabilities of various thiocarbonylthio compounds are compared by measuring the

kinetics under parallel conditions. The concentration of peroxy species, [peroxy], is assumed to be on a steady state at the initial stage. The conversion rate of thiocarbonylthio moiety ($\text{C}(=\text{S})\text{S}$) is expressed by:

$$\ln \left[\frac{[\text{C}(=\text{S})\text{S}]_0}{[\text{C}(=\text{S})\text{S}]_t} \right] = k_{\text{ox}} [\text{peroxy}] t \quad (1)$$

The linearity in kinetic plots in Figures 4 and 5 indicates the applicability of the steady state assumption. Increase the concentration of oxygen results in higher concentration of peroxy radical. Therefore, the reaction in the presence of pure oxygen displays faster rate than that under air, as shown in the case of PEDB (Fig. 4).

It is interesting to find that the reaction rate depends on chemical structure, that is, the structure of leaving (R-) and stabilizing (Z-) groups, of the thiocarbonylthio compounds. For dithioesters with identical Z-phenyl substituent (run 3–7 in Table 1), the conversion rate estimated from the slope in Figure 4 decreases in the order of cyanoisopropyl ($-\text{C}(\text{Me})_2\text{CN}$) > cumyl ($-\text{C}(\text{Me})_2\text{Ph}$) > phenylethyl ($-\text{CH}(\text{Me})\text{Ph}$) > 2-methoxy-1-methyl-2-oxoethyl ($-\text{CH}(\text{Me})-\text{C}(=\text{O})\text{OCH}_3$) > benzyl ($-\text{CH}_2\text{Ph}$). This is surprisingly the same order of the leaving ability of R-group, or chain transfer coefficients of dithioesters, as that previously reported by Rizzardo and coworkers.⁵³ The effect of R-group on the oxidation rate of dithioesters is unexpected because the leaving group is apart from thiocarbonyl sulfur atom by two σ - and one π -bonds. This indicates that the R-group is able to either activate the thiocarbonyl or stabilize the reaction

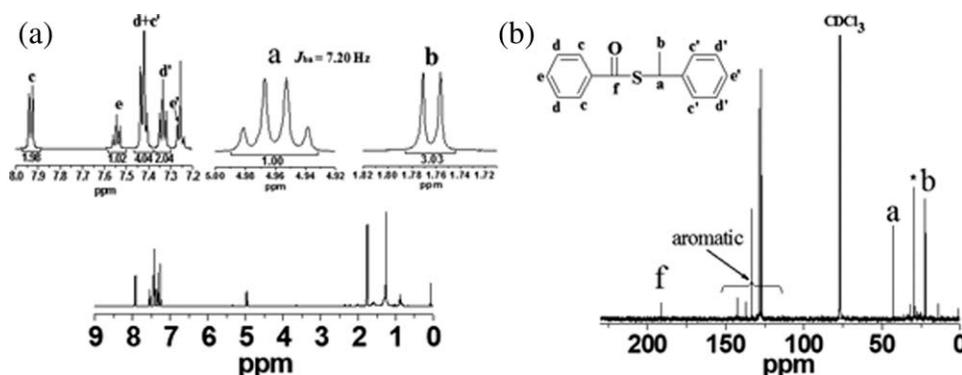


FIGURE 2 ^1H - (a) and ^{13}C - (b) NMR spectra of the oxidation product, PEBT. (The signals with star symbol are from purification solvent, cyclohexane).

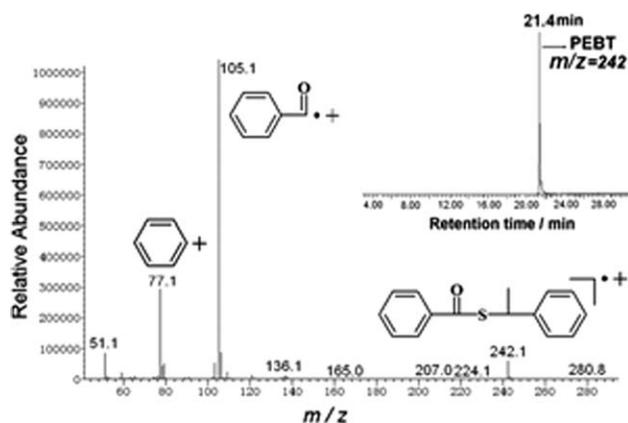
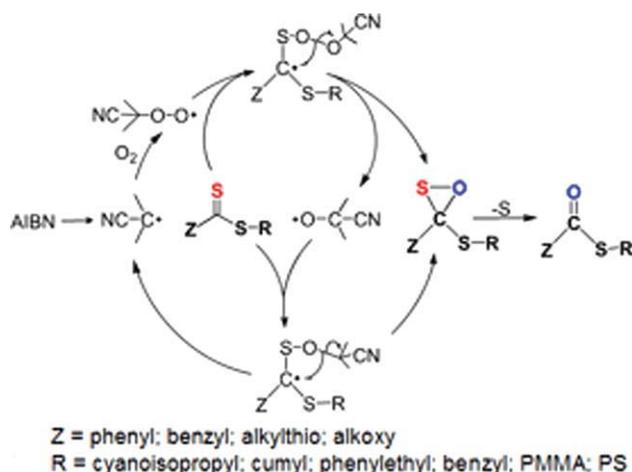


FIGURE 3 Gas chromatography-mass spectroscopy (GC-MS) spectra of PEBT.

intermediate. Because there is no previous report or evidence on the presence and structure (if any) of intermediate in the desulfurization, we will try to explain the fact according to the *ab initio* study^{63–66} on the influence of R-group on the stability of thiocarbonylthio compounds. We hereby assume that the susceptibility of thiocarbonyl toward peroxy radicals is similar to that toward carbon-centered radicals. As pointed out by Coote,⁶³ the substituent can affect the stability of the thiocarbonylthio compound through both electronic and steric factors. A strong electron-withdrawing group, such as cyano group in $-\text{C}(\text{Me})_2\text{CN}$, would reduce the electron donating ability of R-group and, therefore, reduce the stability of C=S bond via the resonance structures (Scheme 2).

Thus, CyDB is most easily oxidized in comparison with other dithioesters. Substituents $-\text{C}(\text{Me})_2\text{Ph}$, $-\text{CH}(\text{Me})\text{Ph}$, and $-\text{CH}_2\text{Ph}$ with different methyl groups affect the stability of thiocarbonylthio compounds by distorting the rigid S=C–S planar system. More bulky substituents lead to more distorted planar system and lower stability of the corresponding compounds.



SCHEME 1 The proposed AIBN-initiated oxidation reaction process of the RAFT agents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

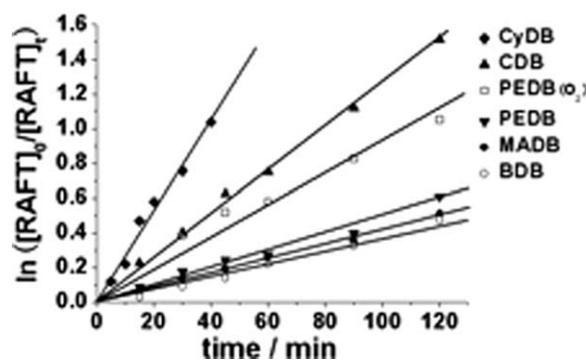


FIGURE 4 Kinetic plots of oxidation reactions for RAFT agents with identical Z (phenyl) group but different R group. The oxidation rate decreased in the order of CyDB ($\text{R} = -\text{C}(\text{Me})_2\text{CN}$) > CDB ($\text{R} = -\text{C}(\text{Me})_2\text{Ph}$) > PEDB ($\text{R} = -\text{CH}(\text{Me})\text{Ph}$) > MADB ($\text{R} = -\text{CH}(\text{Me})-\text{C}(=\text{O})\text{OCH}_3$) > BDB ($\text{R} = -\text{CH}_2\text{Ph}$).

From the results in Table 1 and Figure 5, it is clear that the ease of oxidation is also dependent on the nature of the Z substituent of the RAFT agents. BDB and DBTTC have identical leaving group. The former is completely oxidized within 8 h, whereas the latter needs 38 h. EtoCDB shows the highest stability, reaching a conversion of 73% within 46 h. Thus, the stability of the RAFT agents toward oxidation increases in the order Z = phenyl- \sim benzyl- < RS- (trithiocarbonates) < RO- (xanthates). This again correlates with the reactivity of thiocarbonylthio compounds in the RAFT polymerization,^{67,68} albeit in an inverse order. As previously reported, the apparent chain transfer coefficients of dithioesters with Z = phenyl are in the range of 190–500,^{53,69} while trithiocarbonates is 53.⁷⁰ Xanthates are only effective to more active radicals such as poly(vinyl acetate) propagating radical but unable to mediate the polymerization of styrene and (meth)acrylates.

The agreement between the reactivity of thiocarbonylthio compounds in oxidation and in RAFT polymerization reflects the

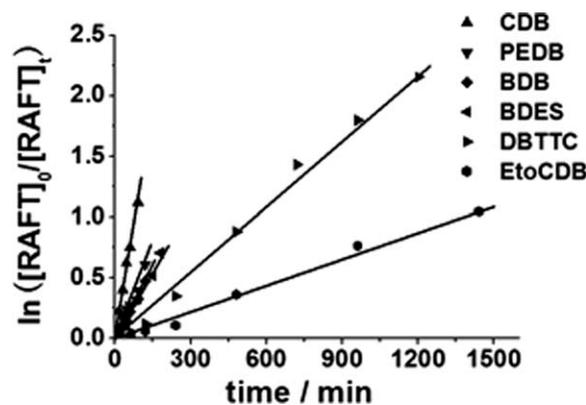


FIGURE 5 Kinetic plots of oxidation reactions for RAFT agents possessing different Z groups. The oxidation rate decreases in the order of PEDB (phenyl dithiobenzoate) \sim BDES (benzyl dithiobenzoate) > DBTTC (trithiocarbonates) > EtoCDB (xanthates).

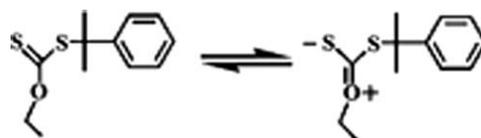


SCHEME 2 The resonance structure of the thiocarbonylthio compound.

electronic feature of molecular orbital. The stabilities of xanthates and trithiocarbonates are associated with the electron donating abilities of lone pair substituents, alkylthio and alkoxy groups, through the resonance structure^{64,67,71–78} (Scheme 3).

The resonance will remarkably raise the energy of LUMO (and HOMO) and reduce the reactivity of C=S toward radical addition.⁶⁷ Indeed, the partial charge on sulfur of the C=S is more negative, as calculated by Rizzardo⁶⁷ and Coote⁶³ using different levels of theory. The strongest deactivating effect is given by alkoxy substituent. Thus, xanthates are the most stable thiocarbonylthio compounds toward oxidation by peroxy radicals. Trithiocarbonates follows but are more stable than dithioesters.

A remarkable feature of the reaction is the high selectivity preferring radical-induced oxidation rather than RAFT process between AIBN-derived cyanoisopropyl radical and thiocarbonylthio compounds. The starting materials are converted nearly completely to thioesters under the reaction conditions. The selectivity may be due to following reasons: (1) The RAFT process of cyanoisopropyl radical with dithioesters is very slow because cyanoisopropyl itself is a much better leaving group than others⁵³; (2) The cyanoisopropyl radical generated from AIBN homolysis is trapped very quickly by molecular oxygen to form the peroxy radical, which will react readily with the C=S group in thiocarbonylthio compound. If the oxidation is carried out in proton-donating solvent, such as THF⁴⁹ or cyclohexane (*vide infra*), thioesters from dithioester precursors formed through the RAFT process with solvent-derived radicals are observed. Therefore, it seems that the property of cyanoisopropyl radical as the best leaving group, and the use of relatively inert solvent, benzene, lead to formation of carbonylthio species free of byproducts and, consequently, facilitate the comparison of oxidation stability of various RAFT agents in the present work.



SCHEME 3 The zwitterionic canonical form of xanthate.

Other radical source, such as alkoxyamine, gives similar results. Heating PEDB and PEET (1-(2,2,6,6-tetramethylpiperidinyl)oxy)-1-phenyl-ethane) in a well-deaerated cyclohexane solution results in no change of HPLC diagram (Supporting Information) because the leaving groups in the reactants are identical. However, in the presence of air, the reaction gives the oxidized product, PEET. The pink color of PEDB fades and the solution becomes light yellow, whereas UV-vis spectrum [Fig. 6(a)] indicates the disappearance of the characteristic absorption band of thiocarbonylthio moiety. In addition, thioester with R-group derived from the solvent, cyclohexyl benzothioate (CHBT), is observed by HPLC [Fig. 6(b)] with the characterization by LC-MS (Fig. 7), GC-MS and NMR (Supporting Information). CHBT is formed through a process similar to that proposed by Barner-Kowollik.⁴⁹ It is interesting to note that the formation of CHBT lags obviously behind the primary oxidation product, PEET. This indicates that peroxy radical, formed from PEET-released phenylethyl radical and oxygen, would attack preferentially thiocarbonyl group rather than cyclohexane. Nevertheless, once a cyclohexyl radical is generated, it will undergo the RAFT process with the residual PEDB, resulting in cyclohexyl dithiobenzoate, which will be quickly oxidized to CHBT.

We have also tried to conduct the oxidation reaction initiated by UV irradiation. Thus, benzene solutions of PEDB and BDES were irradiated by UV of 300–600 nm in the presence of air for 8 h, respectively, then analyzed by HPLC and GC-MS in the same way as that initiated by AIBN. Surprisingly, no oxidized product was observed even after the disappearance of the feed dithioesters, possibly because the oxidation product is decomposed to very low molecular weight species by UV irradiation. Indeed, there is no signal detected in GC as well. Nonetheless, more work should be done after these preliminary results to understand the mechanism of the reaction under UV irradiation.

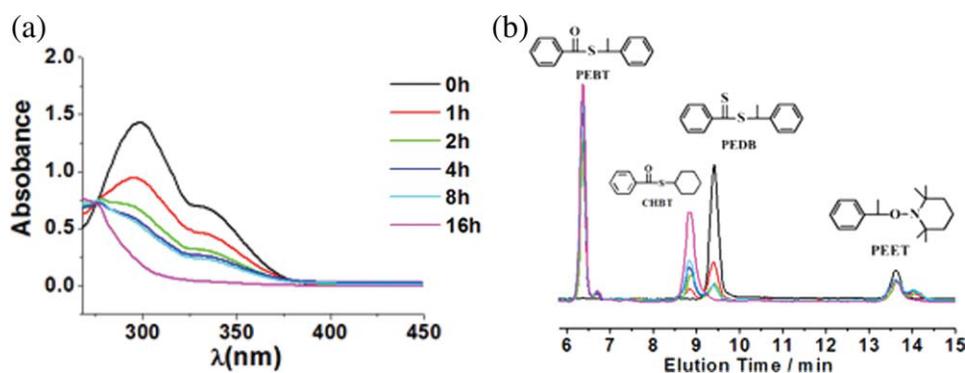


FIGURE 6 UV-vis spectrometry (a) and HPLC (b) monitoring the reaction of PEDB (0.024 g, 0.1 mmol) and PEET (0.032 g, 0.2 mmol) in cyclohexane at 90 °C in the presence of air.

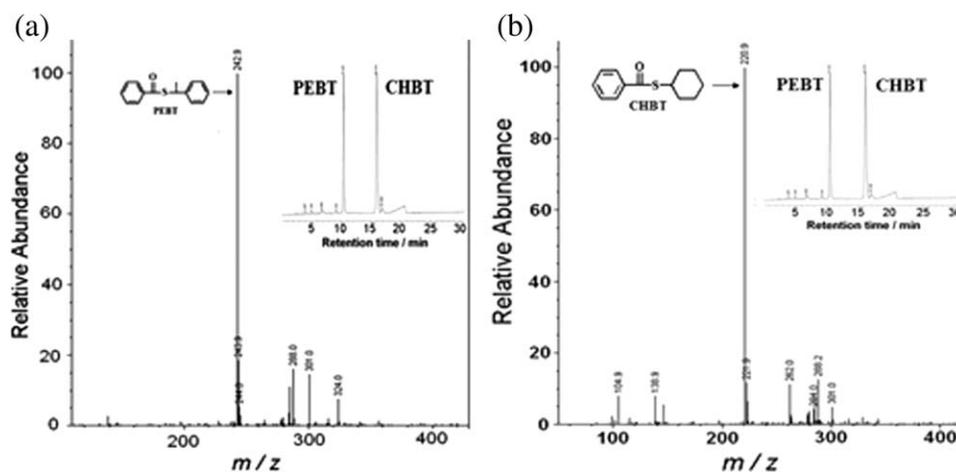


FIGURE 7 LC-MS characterization of the reaction products of PEDB (0.024 g, 0.1 mmol) and PEET (0.032 g, 0.2 mmol) in cyclohexane at 90 °C in the presence of air.

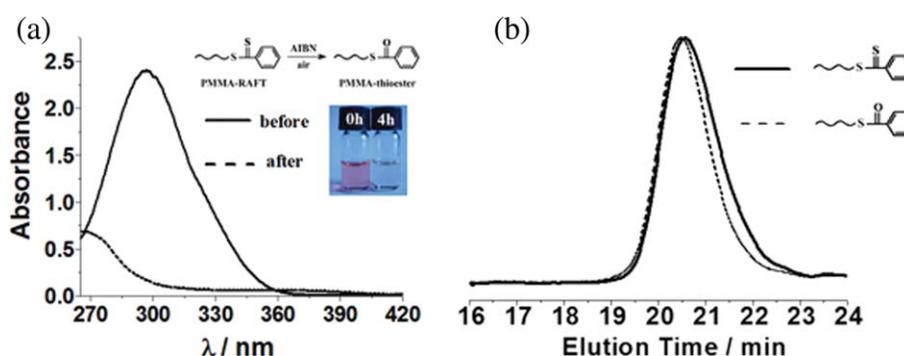


FIGURE 8 UV-vis spectra (a) and GPC diagrams (b) of PMMA-RAFT ($M_n = 2800$ g/mol, $M_w/M_n = 1.14$) before and after heating with AIBN in benzene in the presence of air. Reaction conditions: PMMA-RAFT: 0.28 g, 0.1 mmol; AIBN: 0.065 g, 0.4 mmol, 60 °C for 4 h.

Radical-Induced Oxidation of Dithioesters Terminus of Polymerization Product and Its Effect on RAFT Polymerization

Dithioester terminus of the RAFT polymerization products undergoes oxidation readily as well in the presence of radical and oxygen. Heating polystyrene or PMMA, prepared by cumyl dithiobenzoate-mediated RAFT polymerization, together with AIBN in benzene solution at 60 °C in the presence of air results in rapid oxidation of dithioester moiety as indicated by UV-vis, whereas the polymer molecular weights remain nearly unchanged (Figure 8). In addition, Figure 9 shows the MALDI-TOF MS spectrum of PMMA product, in which the main series (P_1) and a minor series (P_3) are

assignable to oxidized products, for example, PMMA with different ω -end groups but the same thioester terminus (Table 2).

The high content of oxidized product is reminiscent that these species may also be formed readily during the RAFT polymerization system where deaeration has not been well done. This would lead to reduced controllability of the RAFT polymerization. To inspect the issue, two parallel experiments are carried out in which one system is well deaerated before polymerization under nitrogen and the other polymerizes in the presence of air. As shown in Figure 10, the former system seems to polymerize through RAFT process,

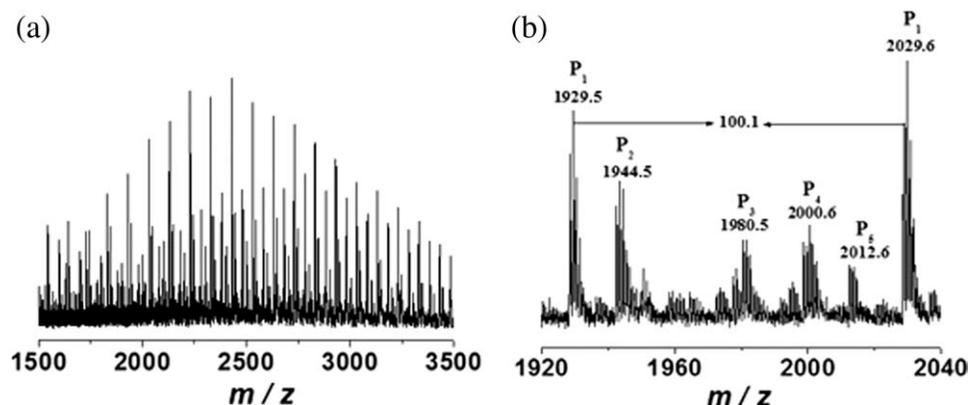
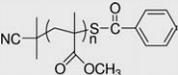
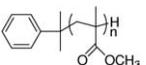
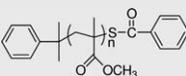
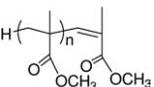
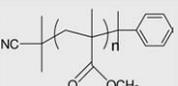


FIGURE 9 Matrix-assisted laser desorption ionization time-of-flight mass spectrum (MALDI-TOF MS) of oxidation product of PMMA-RAFT ($M_n = 2800$ g/mol, $M_w/M_n = 1.14$) in the presence of AIBN and air in benzene. (a: full view, b: partial enlargement.).

TABLE 2 Assignment of Matrix-Assisted Laser Desorption Ionization Time-Of-Flight Mass Spectrum of Oxidation Product of PMMA-RAFT

| Peak | Monoisotopic Mass | | Structure | Ion | Degree of Polymerization |
|----------------|-------------------|--------|---|-----|--------------------------|
| | Exp. | Theo. | | | |
| P ₁ | 1929.4 | 1929.7 |  | Na | 17 |
| P ₂ | 1944.5 | 1944.8 |  | Na | 18 |
| P ₃ | 1980.4 | 1980.7 |  | Na | 17 |
| P ₄ | 2000.4 | 2002.0 |  | H | 20 |
| P ₅ | 2012.6 | 2011.8 |  | Na | 18 |

exhibiting a stepwise increase in molecular weight, whereas the latter exhibits uncontrolled character in which the molecular weight remains nearly constant after an induction period of 4 h. It seems that the RAFT agent has been oxidized during the induction period, as indicated by the color change from pink to light yellow, and the oxidation product causes retardation effect on the polymerization rate. On this base, we suggest that termination by oxidation of the living chains may occur in normal RAFT polymerizations if the system is not well deaerated.

Zhu and coworkers have observed rate-enhancement in RAFT polymerizations of MMA and styrene in the presence of oxygen.⁷⁹ The results are not in contradictory to the present work because of different reaction conditions and different molecular structure of dithioesters. In ref. 79, no radical initiator has been used, and the RAFT polymerization is initiated by the thermal initiation of monomers, in which oxygen plays the role of forming additional peroxide initiators, causing increase in polymerization rate. The oxidation of the RAFT agent may occur at a slow rate due to low concentra-

tion of radicals and limited amount of air in that system. Indeed, they have observed higher polydispersity and tailing effect in GPC profile of the product prepared in the presence of oxygen, which may be a consequence of oxidation termination during the polymerization. In the presence of AIBN, however, remarkable retardation has been observed by Moad et al. for the RAFT polymerization of MMA.⁸⁰

CONCLUSIONS

RAFT agents and dithioester chain terminus are subject to radical-induced oxidation by molecular oxygen. The reaction converts efficiently dithioester moieties to thioester species. The stability of thiocarbonylthio compounds toward oxidation depends on both the structures of Z- and R-substituents. Electron abstracting or bulky group in R-substituent leads to decreased stability, whereas electron-donating group in Z-substituent, such as in trithiocarbonates and xanthates, leads to remarkably increased stability of the compounds. The behavior correlates very well with the chain transfer ability of the RAFT agents. The oxidation of thiocarbonylthio moiety

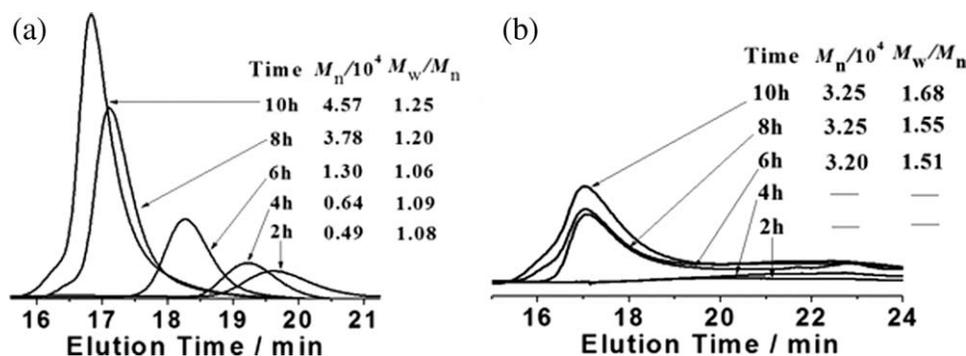


FIGURE 10 GPC traces monitoring the RAFT polymerizations of styrene mediated by PEDB at 60 °C in the absence (a) and presence (b) of air. Feed: styrene: PEDB:AIBN = 2000:1:1 (molar ratio).

exhibits strong competitiveness over the RAFT process therefore is detrimental to the livingness of the polymerization. Understanding the oxidation reaction is of help in obtaining better control on the polymerization.

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