Notes

Effect of Impurities in Cumyl Dithiobenzoate on RAFT-Mediated Polymerizations

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Introduction

Reversible addition−fragmentation chain transfer (RAFT) polymerization is one of the most versatile techniques to produce complex polymer architectures (e.g., blocks, stars, and branched copolymers[1]) with uniform chain length.[2,3] The RAFT mechanism was first proposed by Zard[4] and later confirmed by Rizzardo et al.[5,6] It consists of many complex equilibrium steps, each with an influence on the rate of polymerization and molecular weight distribution. There has been a significant amount of investigation into the effects of inhibition and retardation in RAFT polymerizations.[7−18] The main impetus behind such work is to develop a deep understanding of the complex mechanisms that control the molecular weight distribution and rate of polymerization and therefore enable the technology to be used in the creation of further novel polymer architectures.

The use of cumyl dithiobenzoate (CDB) as a RAFT agent has proven to be a useful agent in obtaining information about additional mechanistic pathways of the RAFT process.[8−12,14] This agent has not exhibited ideal RAFT-mediated polymerization behavior, acting to severely retard or even inhibit the rate of polymerization. Currently, there are two models to describe this behavior: intermediate radical termination (IRT)[8,9] or slow fragmentation.[12] Much of the debate over which model is valid is based on the fit of simulation with experimental conversion vs time data. Feldermann et al.[18] fitted the early times of styrene polymerizations in the presence of CDB and suggested that this together with quantum calculations supported the slow fragmentation model. However, there is a growing body of work that supports the IRT model—ranging from small radical[11,17] to polymeric radical experiments that showed evidence of 3- and 4-arm star formation through the termination of the intermediate radical.[9,11,14] The most critical piece of information that supports the IRT model is that it provides an excellent fit with the intermediate radical concentration as determined from electron spin resonance (ESR).

The aim of this work is to determine the effect of the purity of CDB on the rate of polymerization (i.e., conversion vs time). In particular, we will address the importance of the purification technique, shelf life of CDB, and monomer dependence. It is not the aim of this paper to characterize and elucidate all impurities found in CDB (as this is an impossible task) but to determine whether the purity of CDB has implications on mechanistic conclusions of the RAFT process. It has been recently reported by Favier et al.[19] that possible byproducts from the synthesis of xanthate RAFT agents produced an inhibition period in the polymerization of vinyl acetate, providing strong evidence that impurities are a necessary concern. Obviously, there are many other factors that would influence the rate of polymerization, including oxygen (deoxygenation procedure), residual inhibitor in the monomer, purity of monomer, solvent, solvent purity, initiator purity, and many more, all of which will play some role, be it large or small, on the rate of polymerization.

Results and Discussion

Effect of CDB Purity on the Rate of Polymerization. The general literature procedure used in most RAFT studies to purify CDB is by passing it through a silica column.[13] We have denoted this as CDB-Si. Elemental analysis of this gave a purity of ≈97% and when analyzed using HPLC showed many residual peaks. To determine the effect of the purity of CDB, we further purified CDB-Si through preparative HPLC to remove many of the residual peaks (denoted as CDB-HPLC). The elemental analysis of CDB-HPLC gave a calculated purity of >99%.

The first set of polymerizations was carried out using 2-hydroxyethyl methacrylate (HEMA) in the presence of CDB-Si (2.6×10^{-2} M, used immediately after silica column purification, curve a) and CDB-HPLC (stored for 1 week at −20 °C, curve b), which was initiated with 2,2-azobis(isobutyronitrile) (AIBN, 3.5×10^{-3} M) at 60 °C. Figure 1, curve a, shows the conversion vs time data for the HEMA polymerization using CDB-Si as monitored by Fourier transform infrared spectroscopy (FT-IR), which is highly accurate at low conversion where monomer concentration is high. There is an initial inhibition period lasting ≈100 min and then an increase to 63% conversion after 1205 min. Purification of the CDB by HPLC (CDB-HPLC) gave a shorter inhibition period of approximately 10 min (Figure 1, curve b) and a rate of polymerization that was much faster, reaching a conversion of 90% after the same time (1205 min). This suggests that impurities in CDB cause both inhibition and retardation in the rate of a HEMA RAFT-mediated polymerization.

The effect of CDB purity of the RAFT-mediated polymerization of styrene initiated with AIBN ($4.5 \times$

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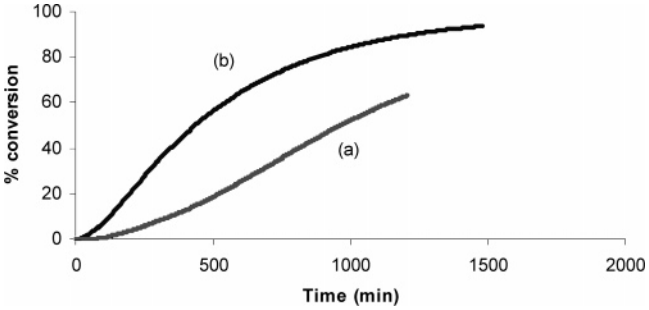

Figure 1. Conversion vs time plots for the polymerization of 2-hydroxyethyl methacrylate (HEMA, 2 M) in the presence of cumyl dithiobenzoate (CDB, 2.6×10^{-2} M), 2,2-azobis(isobutyronitrile) (AIBN, 3.5×10^{-3} M), and DMF solvent at 60 °C. (a) CDB was purified using a Si column and was one spot by thin-layer chromatography, and (b) CDB after Si column purification was further purified using preparative HPLC until only one peak was observed and used after 1 week storage at −20 °C.

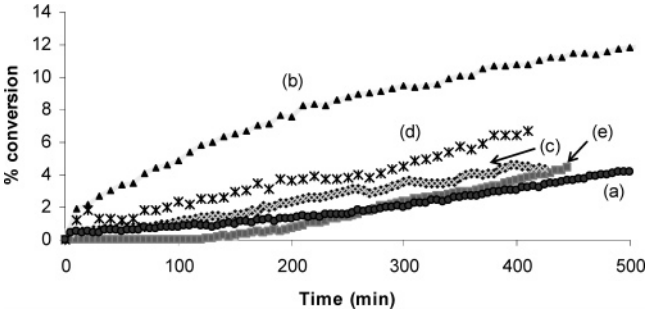

Figure 2. Conversion vs time plots for the polymerization of styrene at 60 °C in the presence of 2,2-azobis(isobutyronitrile) (AIBN, 4.5×10^{-3} M), using cumyl dithiobenzoate (CDB, 2.1×10^{-2} M): (a) silica purified CDB (used immediately after purification), (b) HPLC pure CDB (stored for 1 week at −20 °C), (c) HPLC pure CDB (stored for 3 months at −20 °C), (d) HPLC pure CDB (stored for 9 months at −20 °C), and (e) HPLC pure CDB (stored for 3 months at −20 °C) with added dithiobenzoic acid (DTBA, 2 wt % to CDB).

10^{-3} M) at 60 °C is given in Figure 2, using CDB-Si (2.1×10^{-2} M, used immediately after silica column purification, curve a) or CDB-HPLC (stored for 1 week at −20 °C, curve b). Curve a shows that the rate of styrene polymerization in the presence of CDB-Si was very slow up to 135 min (conversion was less than 1%), after which conversion reached 4.2% after 500 min. The use of the more pure CDB-HPLC (curve b) showed no observable inhibition period, and the conversion reached 12% after 400 min.

To determine whether storage of CDB-HPLC would affect the rate, the next set of polymerizations were carried out with CDB-HPLC stored at −20 °C for 3 and 9 months (see Figure 2, curves c and d, respectively). The reason for using HPLC grade CDB was to determine whether CDB alone could degrade to form products that would affect the rate of polymerization. The storage time of 3 and 9 months seemed to lower the rate in comparison to storage of 1 week (curve b), but there was a slight increase in rate for CDB-HPLC stored for 9 months. This is surprising as the reverse would be expected. It is believed that the experimental error when measuring conversion by FT-IR is close to ±1%, which suggests that prolonged storage has little or no effect on the rate after 3 months.

To determine whether impurities in CDB would affect other monomer systems, we compared the effect of CDB purity in a methyl acrylate (MA) system. Figure 3, curve

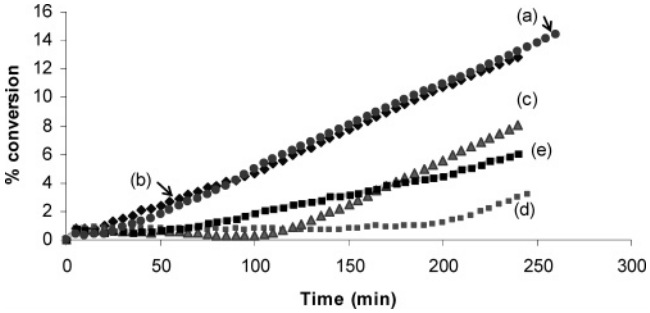

Figure 3. Conversion vs time plots for the polymerization of methyl acrylate (MA) in the presence of 2,2-azobis(isobutyronitrile) (AIBN, 3.5×10^{-3} M), using cumyl dithiobenzoate (CDB, 3.8×10^{-3} M) with varying amounts of dithiobenzoic acid (DTBA) at 60 °C: (a) silica purified CDB (used immediately after purification), (b) HPLC pure CDB (stored for 1 week at −20 °C), (c) HPLC pure CDB (stored for 1 week at −20 °C) with added dithiobenzoic acid (DTBA, 3.9 wt % to CDB), (d) HPLC pure CDB (stored for 1 week at −20 °C) with added dithiobenzoic acid (DTBA, 24 wt % to CDB), and (e) HPLC pure CDB (17.4×10^{-3} M, stored for 1 week at −20 °C).

a, shows the polymerization of MA in the presence of CDB-Si (3.8×10^{-3} M) that was initiated with AIBN (3.5×10^{-3} M) at 60 °C. These are the same experimental conditions used by Perrier et al.[7] There is a very low rate of polymerization lasting ≈25 min, after which conversion increases linearly with time, reaching a conversion of 14.5% after 260 min. The polymerization with CDB-HPLC (stored for 1 week at −20 °C, Figure 3, curve b) showed a shorter inhibition period of ≈10 min, reaching a conversion of 13% after 240 min. The rates using the silica purified and HPLC purified CDB are very similar after the initial inhibition periods, suggesting that MA is only inhibited by such impurities. Surprisingly, these results are in contrast to the rates observed by Perrier et al.,[7] where they stated that CDB at 60 °C inhibited the polymerization of MA completely, even though they used CDB with a similar purity (98%). They also suggested that the 2% residual impurity was due to hexane (from the chromatographic eluent), but we find from our HPLC analysis that these residual impurities are composed of many compounds. An increase in the CDB-HPLC concentration to 17.4×10^{-3} M (curve e) showed that the rate was much lower than at the lower concentration of 3.8×10^{-3} M, which suggests that retardation is dependent upon CDB concentration (the larger the concentration of CDB, the greater the retardation in rate).

These results highlight the strong monomer dependence of CDB purity on the rate of polymerization for styrene, HEMA, and MA. Storage of CDB-HPLC in the styrene system should also be considered. On the basis of these results, we believe that in kinetic studies of RAFT-mediated polymerizations, e.g., styrene and HEMA, freshly HPLC purified CDB should be used. Failure to do so could lead to erroneous mechanistic conclusions, especially when trying to fit the early time data to a model.

Although the number of impurities in CDB is large and of wide ranging molecular composition, dithiobenzoic acid (DTBA) was one of the compounds identified in the HPLC chromatogram. The elution times of DTBA and CDB were approximately 15.8 and 16.2 min, respectively. As a result, it would be difficult to completely remove DTBA from CDB after preparative HPLC. We therefore wanted to determine the effect of

Table 1. Comparison between Experimentally Determined Inhibition Times and Theory Using an Initiator Efficiencies of 0.6 and 1 for All Monomers Used in This Study

					inhibition time (min) theory[e]	
monomer	[CDB] (M)	AIBN (M)	DTBA (wt % to CDB)	inhibition time (min)	$f = 1$	$f = 0.6$
HEMA	2.6×10^{-3} [a]	3.5×10^{-3}	0	10		
	2.6×10^{-3} [b]	3.5×10^{-3}		120		
styrene	2.1×10^{-2} [a]	4.5×10^{-3}	0	0		
	2.1×10^{-2} [c]	4.5×10^{-3}	0	0		
	2.1×10^{-2} [d]	4.5×10^{-3}	0	0		
	2.1×10^{-2} [c]	4.5×10^{-3}	2	150	151	260
MA	3.8×10^{-3} [a]	3.5×10^{-3}	0	0		
	3.8×10^{-3} [a]	3.5×10^{-3}	3.9	100	69	117
	3.8×10^{-3} [a]	3.5×10^{-3}	24	200	477	886
	17.8×10^{-3} [a]	3.5×10^{-3}	0	50		

[a] HPLC pure CDB used after 1 week storage. [b] Silica gel column purified. [c] HPLC pure CDB stored for 3 months at −20 °C. [d] HPLC pure CDB stored for 9 months at −20 °C. [e] $t_{\text{inhib}} = \{\ln[(1 - ([\text{DTBA}]/2f[\text{I}]_0]\}/-k_{\text{d}}$.

DTBA on the rate of polymerization. Bai et al.[20] had studied the effects of styrene and MA polymerizations in the presence of DTBA. Unfortunately, they provided little information on the conversion vs time profiles for MA and no data for styrene at 60 °C. In addition, they did not test it as an impurity in a CDB RAFT-mediated polymerization. However, they found that the number-average molecular weight (M_{n}) increased linearly with conversion in accord with the theoretically calculated values and found polydispersities that were low (below 1.2) at 60 and 80 °C. They postulated that this was due to DTBA reacting with monomer to form the corresponding RAFT agent.[21]

The purity of DTBA used in this study as determined by elemental analysis was 93.9%, and there are numerous other peaks in the HPLC chromatogram. To determine the effect of this starting reagent on the rate of polymerization, DTBA (2 wt %) to CDB was added in the presence of CDB-HPLC in a styrene polymerization initiated with AIBN at 60 °C (Figure 2, curve e). There is an observed inhibition period lasting for 150 min, after which the rate of polymerization is similar to the CDB-HPLC stored for 3 and 9 months. The addition of 3.9 and 24 wt % DTBA to CDB (Figures 3, curves c and d, respectively) to the polymerization mixture of MA in the presence of CDB-HPLC initiated with AIBN (3.5×10^{-3} M) at 60 °C shows that the inhibition period increased from approximately 100 to 200 min with increasing DTBA. After the inhibition time, the rate of polymerization for 3.9 and 24% DTBA is similar to that without DTBA (curve a). These results show that as the weight fraction of DTBA is increased so to is the inhibition time, strongly suggesting that DTBA or the 6% impurities found in DTBA act to inhibit the polymerization of styrene and MA.

The theoretical inhibition times, determined assuming DTBA as the sole inhibitor, are much greater than that found from experiment (Table 1). The theoretical inhibition time was calculated from the loss of AIBN in which the cumulative radical concentration equals the concentration of added DTBA and using an initiator efficiency, f, of 0.6. These results suggest that the mechanism of inhibition with the addition of DTBA is not obvious and is complicated by a number of other factors. These completing factors could possible include (i) degradative chain transfer, (ii) 6% impurities found in DTBA, (iii) stability of DTBA, which may decompose or oxidize to compounds (e.g., disulfides), (iv) reaction of DTBA with monomer to form the corresponding RAFT agent,[21] and many other possible side reactions. The mechanism of degradative chain transfer is through the process of first the transfer of a hydrogen from DTBA[22] to form the incipient radical, •SC(Ph)═S, which reacts very slowly toward monomer and has a high probability of terminating with radicals in the system, resulting in inhibition of polymerization. Impurities in DTBA could both increase the rate through the creation of radicals or inhibit the rate through the presence of compounds that act as inhibitors or retarders. DTBA could also be lost through the reaction with monomer (iv), resulting in a lower amount of DTBA and thus a lower amount of inhibitor. However, the reaction of DTBA with MA is a slow process[21] (∼24 h at 70 °C), and thus the loss of DTBA via this reaction could be neglected on the basis of polymerization times (∼4 h). We believe that even through a more detailed study the true inhibition mechanism may not be fully elucidated, primarily due to the high number and low quantities of impurities in the polymerization mixtures.

Conclusion

These results clearly show that the impurities in cumyl dithiobenzoate act to inhibit or retard the polymerization of HEMA, styrene, and MA. The addition of the starting reagent DTBA also acts to inhibit the polymerization. However, the mechanism for this is not obvious. These findings highlight the fact that trying to determine the mechanism operating in the early polymerization time region is much more complex than considering only leaving group reactivity toward monomer, rate of fragmentation, or intermediate radical termination. Therefore, caution should be taken especially when trying to distinguish between models or to simulate the polymerization at early times in a RAFT-mediated polymerization. These results could in part explain the anomalous behavior observed in the ESR after 3 min, in which they observed complex hyperfine structure, as found by Chernikova et al.[23]

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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