Ionic Dithioester-Based RAFT Agents Derived from N-Heterocyclic Carbenes

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Over the past 15 years, controlled radical polymerizations,[1] such as atom transfer radical polymerization,[2] nitroxide mediated polymerization,[3] and reversible addition−fragmentation chain transfer (RAFT) polymerization,[4] have emerged as powerful methods for preparing polymeric materials with predetermined molecular weights and low polydispersities.[5] Since initial reports[6] in the late 1990s, RAFT and related[7] polymerizations have experienced tremendous growth. As a result of their versatility and compatibility with a broad range of monomers and solvents, these techniques have found utility in many facets of macromolecular chemistry, including aqueous polymerizations and the synthesis of advanced materials with useful functions.[8,9]

RAFT polymerizations typically employ specialized chain transfer agents (CTAs)[10] that facilitate the transfer of relatively few propagating radical species among many growing polymer chains.[11] As a result, deleterious bimolecular termination pathways are effectively minimized, which enables all chains to grow in a uniform fashion. Of the various types of CTAs known, which include trithiocarbonates, dithiocarbamates, xanthates, and dithioesters, the latter have been used extensively. Effective dithioester-based RAFT agents with the general structure S═C(Z)−SR share two design features: (1) benzyl, cumyl, 2-cyanopropyl, or other R groups that afford a stable radical upon undergoing homolytic cleavage from the dithio moiety[12] and (2) a Z group that balances sufficient electrophilicity toward radical addition with efficient fragmentation.[13] In general, RAFT agents with electron-rich Z groups facilitate fragmentation but disfavor radical addition, a feature that has found utility in polymerizing vinyl acetate.[14] In contrast, electron-deficient Z groups favor radical addition but afford highly stable intermediates that resist fragmentation which often leads to relatively long polymerization reactions. Since the general features required to facilitate radical addition oppose those required for efficient fragmentation, the key to an active and broadly useful RAFT agent is to find a Z group that offers an optimal balance. Dithiobenzoates are excellent examples because aryl Z groups (particularly Z = phenyl) balance radical stability with propensity toward fragmentation; as such, they offer control over a wide range of monomers.[4,10,11]

As illustrated in Scheme 1, we envisioned a 2-carbodithioimidazolium salt capable of intermittently delocalizing positive charge onto the dithioester moiety through conformational change. In particular, coplanarization of the dithioester and imidazolium moieties should result in a system with a low-energy LUMO poised for radical addition. Since the resulting radical species is pseudo-benzylic, it should be relatively stable. However, rotation about the imidazolium−dithioester bond should diminish electronic communication between these two groups and afford a relatively destabilized radical species primed for fragmentation. Considering the rotational barrier will be influenced by sterics, we ultimately envision fine-tuning these processes by varying the size of the N-substituents. Herein, we disclose our initial results toward realizing this concept. In particular, the syntheses of two new dithioester-based RAFT agents containing imidazolium Z groups and their potential in controlling free radical polymerizations are described. A fundamental corollary of our investigation was to explore the effect of placing a positive charge in close proximity to the dithioester moiety on polymerization activity which, to the best of our knowledge, has not been previously studied in detail.[15]

Syntheses of the aforementioned imidazolium-based dithioesters are summarized in Scheme 2 and capitalize on the chemistry of N-heterocyclic carbenes,[16] a versatile class of compounds finding tremendous utility in catalysis[17] and as monomers for polymer synthesis.[18] Treatment of commercially available 1,3-dimesitylimidazolylidene (**1**) with excess carbon disulfide in tetrahydrofuran (THF) afforded inner salt **2** in 99% yield after 2 h at ambient temperature.[19] Subsequent alkylation of **2** with benzyl bromide at 85 °C in acetonitrile afforded benzyl 1,3-dimesitylimidazolium-2-carbodithioate bromide (**3**) in 93% yield. No chromatography, distillation, or other elaborate purification procedures were required in these reactions; rather, the products were isolated using straightforward filtration techniques.[20]

To confirm the molecular structure of **3**, a crystal was grown by slow evaporation of a saturated ethyl acetate solution and analyzed by X-ray diffraction. As shown in the ORTEP diagram in Figure 1, the dithioester moiety is nearly orthogonal to the plane of the imidazolium species (avg abs N−C−C−S ≈ 71°). This observation suggested to us that electronic communication between the dithioester and imidazolium moieties was restricted in the solid state. However, the rotational barrier about the dithioester−imidazolium bond in **3** was calculated[21] to be less than 7 kcal/mol, suggesting that an appreciable population of the coplanar conformation should exist in solution, particularly at elevated temperatures.

Upon synthesis and characterization of **3**, efforts were directed toward exploring the ability of this compound to mediate the polymerization of styrene.[22] Initially, 0.96 mmol of **3** and 0.19 mmol of 2,2′-azobis(isobutyronitrile) (AIBN) were dissolved in 1.1 mL of degassed styrene (monomer:CTA:AIBN = 200:5:1). A small amount of an internal standard (i.e., 1,2,3-trimethoxybenzene) was included in the reaction mixture to help monitor the conversion of monomer to polymer. After heating at 110 °C under an atmosphere of nitrogen for 72 h, no polymer was observed by ^{1}H NMR analysis of the crude reaction mixture which indicated to us that **3** was highly effective at limiting propagating radical species.[23] To facilitate polymerization, the CTA:AIBN ratio was reduced to 1:1, and the aforementioned polymerization experiment was repeated. After 24 h at 110 °C, 87% of monomer was consumed, and polystyrene with a number-average molecular weight (M_n) of 19.1 kDa, as determined by gel permeation chromatography,[24] was obtained. The M_n of the polymer was in good agreement with its theoretical molecular weight of 18.7 kDa, which was based on monomer conversion and complete incorporation of **3**.[25] Unfortunately, the chromatograms of these polymers showed significant tailing, and bimodal distributions were observed at higher conversions.

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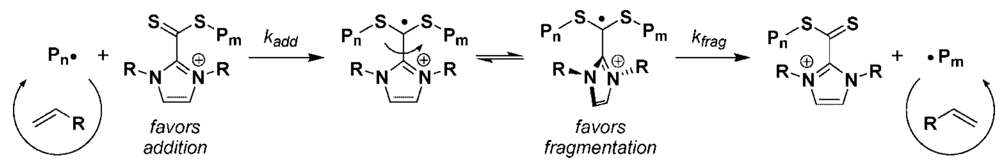
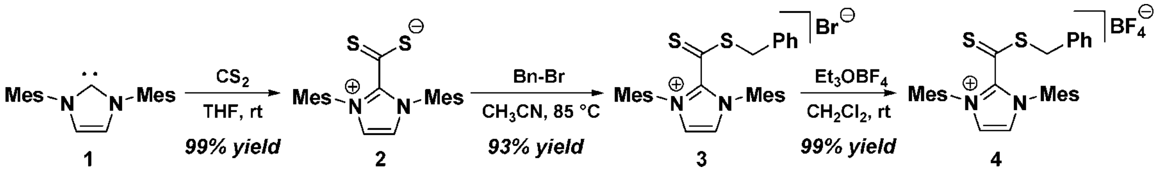
Scheme 1. Proposed Concept of Using Cationic Dithioesters To Control Key Radical Transfer Processes in RAFT Polymerizations (Counteranions Have Been Omitted for Clarity)



Scheme 2. Synthesis of Ionic RAFT Agents 3 and 4 (Mes = 2,4,6-Trimethylphenyl, rt = Room Temperature)



To circumvent these deleterious issues, polymerizations were attempted at lower temperatures but were ultimately hampered by the limited solubility of **3** in styrene.

Considering the complementary reactivity of the nucleophilic bromide anion and the eletrophilic benzyl group in **3**, we postulated that this compound most likely decomposes via an S_N2-type process under the aforementioned polymerization reaction conditions. To investigate, solutions of **3** were heated to 100 °C in either DMSO-d_6 or chlorobenzene[26] and monitored over time by ^{1}H NMR spectroscopy. Although **3** was found to decompose in both solvents, the relative decomposition rates were highly dependent on the solvent polarity. For example, in DMSO-d_6, **3** was found to fully decompose within 3 h but required >20 h in chlorobenzene to achieve complete decomposition. Extrapolating this reactivity, we suspect the decomposition of **3** would proceed even slower in bulk styrene, a relatively nonpolar solvent that disfavors S_N2-type chemistry. However, the limited solubility of this compound in less polar solvents (i.e., C_6D_6 or toluene-d_8) prevented verification of this hypothesis.

In an effort to minimize decomposition, the nucleophilic bromide counteranion was exchanged for a tetrafluoroborate via anion metathesis. This transformation was accomplished by treating a CH_2Cl_2 solution of **3** with a slight excess of triethyloxonium tetrafluoroborate at room temperature,[27] which afforded **4** as a pink powder in >99% yield. Gratifyingly, compound **4** showed improved solubilities in nonpolar organic solvents, including styrene, and exhibited no signs of decomposition in chlorobenzene,[26] $CDCl_3$, toluene-d_8, or styrene[26] at 100 °C for at least 48 h. In DMSO, however, ~15% of **4** was found to decompose over the same period of time.

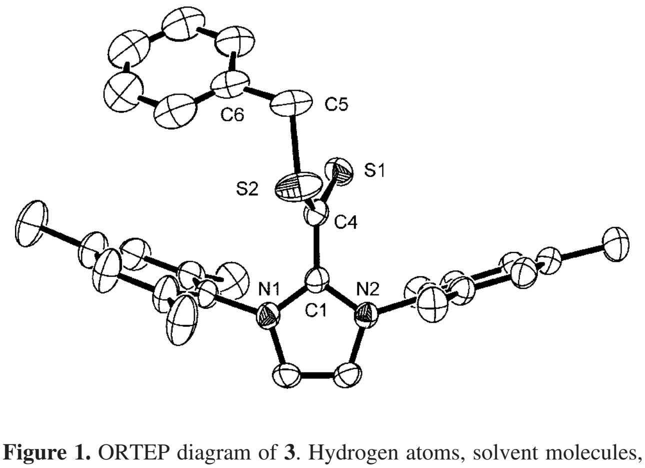


Figure 1. ORTEP diagram of **3**. Hydrogen atoms, solvent molecules, and counterions have been removed for clarity. Ellipsoids were drawn at the 50% probability level. Selected distances (Å) and angles (deg): N1–C1, 1.339(4); N2–C1, 1.344(4); C1–C4, 1.484(4); S1–C4, 1.623(6); S2–C4, 1.703(5); S2–C5, 1.804(6); N1–C1–N2, 107.9(2); C1–C4–S1, 121.0(4); S1–C4–S2, 125.6(5); C4–S2–C5, 103.9(4); C6–C5–S2, 114.2(11); N1–C1–C4–S1, −114.5(7); N1–C1–C4–S2, 74.2(6); N2–C1–C4–S1, 68.7(7); N2–C1–C4–S2, −102.6(6); C1–C4–S2–C5, −173.0(10); C4–S2–C5–C6, 76.6(8).

Poised by these favorable physical and thermal properties, **4** was explored for its ability to mediate the polymerization of styrene. Using reaction conditions similar to those described above (i.e., styrene:**4**:AIBN = 200:1:1), a polystyrene with a number-average molecular weight (M_n) of 19.6 kDa and a polydispersity index (PDI) of 1.26 was obtained in 84% isolated yield after 22 h at 70 °C. The experimentally determined M_n was in good agreement with its theoretical value of 18.1 kDa, which was based on monomer conversion and complete incorporation of the CTA into growing polymer.[25] To gain support for the latter, we capitalized on the BF_4 counteranion associated with **4**, which presumably should also be associated with its respective polymer. Indeed, analysis of the aforementioned polymer by ^{19}F NMR spectroscopy revealed two distinct signals at δ −152.6 and −152.7 ppm in a 1:4 ratio, respectively, which were in accord with the isotopic distribution of boron and at similar chemical shifts as the BF_4 anion in **4**. A solution of this polymer was then spiked with a known quantity of 1,2,4,5-tetrafluorobenzene (δ −138.7 ppm), and the resulting mixture was analyzed using ^{19}F NMR spectroscopy. Integrating the ^{19}F NMR signals attributed to the standard relative to those attributed to the BF_4 revealed that these two species were present at a ratio of 55:45, respectively. Using the known concentration of the standard, the M_n of the polymer was calculated to be 16.6 kDa, which is in good agreement with the value obtained by GPC. In other words, using this method, each polymer chain appears to contain approximately one CTA.

An ability to prepare well-defined polymers with relatively low CTA:AIBN ratios was unusual since RAFT polymerizations typically employ ratios of up to 10:1 in order to maintain control. Despite the low ratio, key characteristics of a controlled/"living" polymerization were observed. For example, as shown in Figure 2, monitoring a bulk polymerization of styrene mediated by **4** using a CTA:AIBN = 1:1 revealed (A) pseudo-first-order kinetics with respect to monomer as evidenced by the linear correlation between the log monomer concentration and time and (B) a linear relationship between polymer molecular weight and monomer conversion while polydispersity remained low (<1.3). Representative GPC chromatograms for a typical

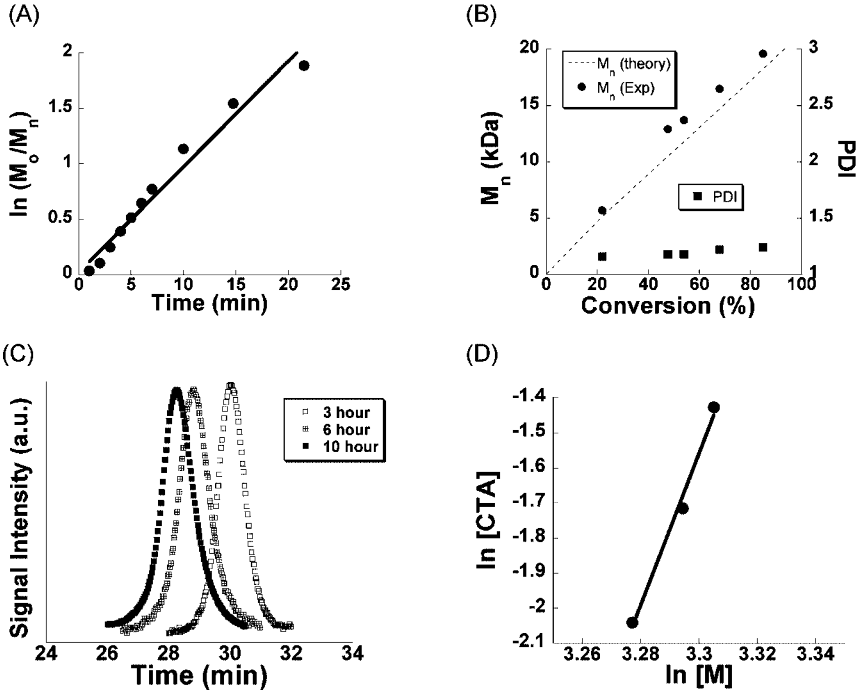


Figure 2. (A) Plot of log monomer concentration vs time. (B) Plot of M_n (experimental[24] and theoretical[25]) and PDI vs monomer conversion. (C) GPC chromatograms taken at 4, 7, and 10 h. (D) Double-log plot of [CTA] vs [styrene] used for determination of C_{tr}. The slope to this curve was found to be 22. Conditions: $[\mathbf{4}]_0 = 48$ mM, $[\text{AIBN}]_0 = 48$ mM, $[1,2,3\text{-trimethoxybenzene}]_0 = 295$ mM (internal standard), bulk styrene, 70 °C (monomer:CTA:AIBN = 200:1:1).

polymerization of styrene using **4** as a CTA are shown in Figure 2C.

Considering AIBN decomposes into two isobutyrylnitrile radicals, the aforementioned results suggested to us that a single unit of **4** is capable of mediating multiple radical species. This unique ability may be at least partially explained by highly favored radical addition to the CTA coupled with efficient fragmentation. To gain additional insight into this process, the chain transfer constant (C_{tr}), which reflects the ability of **4** to facilitate radical addition, was determined by ^{1}H NMR analysis to be 22 (Figure 2D).[12] This C_{tr} value is similar to that derived for dibenzyl trithiocarbonate,[13] an effective CTA for mediating RAFT polymerizations. Hence, to rationalize the results observed, we surmise that **4** exhibits higher absolute rates of addition and fragmentation than dibenzyl trithiocarbonate.

In summary, we have synthesized two new ionic dithioester-based CTAs and studied their abilities to mediate free radical polymerizations of styrene. Starting with a commercially available N-heterocyclic carbene, these agents were synthesized in two or three high yielding steps that required only straightforward filtration techniques for isolation. These compounds were found to be effective for preparing well-defined polystyrenes at relatively low CTA:initiator ratios. Considering the breadth of imidazole chemistry, the methodology reported herein should facilitate access to RAFT agents that are highly functionalized or exhibit tunable activities through judicious N-substitution, electronic modulation of the N-heterocyclic carbene component, or variation of the counteranion. Efforts along these lines are in progress and will be reported in due course.

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Supporting Information Available: Additional experimental details and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) As controls, polymerizations were performed in the absence of AIBN using various styrene:CTA ratios (up to 200:1). After 2 days at 110 °C, no polymer was observed when either **3** or **4** was used as the CTA. These results suggested to us that AIBN was essential for forming active radicals and hence polymer.

(24) Molecular weights and polydispersities were determined using gel permeation chromatography (eluent = DMF/LiBr or THF) and are reported relative to polystyrene standards.

(25) $M_{\mathrm{n,theory}} = ([\mathrm{mon}]_0/[\mathrm{CTA}]_0) \times \mathrm{FW}_{\mathrm{mon}} \times \%\ \mathrm{mon\ conv} + \mathrm{FW}_{\mathrm{CTA}}$.

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