Controlled Radical Polymerization

Reaction of Cyclic Tetrathiophosphates with Carboxylic Acids as a Means to Generate Dithioesters and Control Radical Polymerization By RAFT[**]

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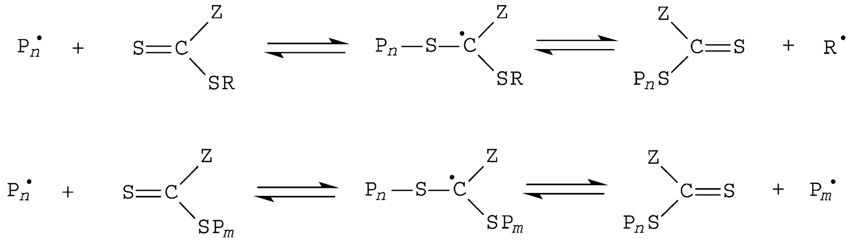
Substantial research has been devoted in recent years to controlled radical polymerization (CRP).[1] The CRP methods combine the advantages of truly "living" systems with regard the quality of the polymers formed with the inherent ease of radical processes.[1] Among the CRP systems, nitroxide-mediated polymerization (NMP),[2] atom-transfer radical polymerization (ATRP),[3] and reversible addition fragmentation chain transfer (RAFT)[4] have been extensively investigated. However, all of these methods have drawbacks that limit their industrial development. For example, NMP often requires elevated temperatures and is only applicable to a limited number of monomers,[2] and ATRP, though very powerful, is ineffective for monomers that can poison the catalyst (e.g., acrylic acid, acrylamide); moreover, the removal of metal ions from polymers is an unresolved issue on the industrial scale.[3] As to the RAFT process, the preparation of the corresponding chain-transfer agents suffers from drawbacks, such as the use of carbon disulfide or iodine, two toxic reagents.[4] This situation shows the necessity to improve CRP methods before they can be implemented in industry.

Herein we describe the preparation of dithioesters by reaction of Davy reagents or P_4S_{10} with benzoic acid. These dithioesters serve to control in situ the free-radical polymerization of styrene and alkyl (meth)acrylates. Davy reagents and P_4S_{10} are commercially available cyclic tetrathiophosphates that are widely employed for the thionation of carbonyl groups and the preparation of thioamides, thiopeptides, thiolactams, and dithioesters.[5–9] Our aim is to provide an efficient, single-step procedure to access well-defined polymers by generating RAFT agents in situ. A major advantage of our approach is that polymerization can be initiated and controlled by chain-to-chain transfer of ω-thiocarbonylthio groups (Scheme 1)[4] without isolating any intermediates.

Styrene was first polymerized in the bulk at 110 °C in the presence of P_4S_{10} and PhCOOH in a one-pot procedure. After 50 h this afforded a polystyrene (PS) sample with $M_n = 5800\,\mathrm{g\,mol^{-1}}$ and a polydispersity index (PDI) of 1.4 (34% conversion). A similar reaction involving styrene, P_4S_{10}, and PhCOOH was also performed at 60 °C with azobis(isobutyronitrile) (AIBN), as a radical source. This vastly improved control over the polymerization: a PS sample with $M_n = 3300\,\mathrm{g\,mol^{-1}}$ and PDI = 1.11 was obtained after 16 h (19% conversion). To explain these differences, we hypothesized that the reaction between PhCOOH and P_4S_{10} generated dithiobenzoic acid (DTBA) as an intermediate (Scheme 2). Dithiobenzoic acid is usually prepared by reaction of bromobenzene with magnesium and subsequent treatment with CS_2 and aqueous HCl.[10,11] Dithioic acids, such as DTBA, add to substituted alkenes to form dithioesters. Depending on the electron density of the alkene, the addition can either result in a Michael-type reaction (path B) or follow a Markownikoff-type mechanism (path A).[12,13] Therefore, it is likely that the reaction between PhCOOH and P_4S_{10} first generated DTBA, which subsequently added to styrene to give phenylethyl dithiobenzoate (path A in Scheme 2). Such a dithioester, formed in situ, then acted as a chain-transfer agent (CTA) and controlled the RAFT polymerization of styrene.



Scheme 1. Z = alkyl or aryl, OR, NR^2R^3, SR^4.

Next, P_4S_{10} and PhCOOH were heated together in toluene, and the product formed was treated with NaH and bromopropionyl bromide. Propionyl dithiobenzoate was formed (path D in Scheme 2).

To account for the role of AIBN in the polymerization carried out at 60 °C, a mixture of PhCOOH, P_4S_{10}, and AIBN was heated in toluene at 110 °C (no monomer was added). After workup, cyanopropan-2-yl dithiobenzoate was recovered, as demonstrated by ^{1}H NMR spectroscopy. This dithioester was formed by the radical path C in Scheme 2.[14,15] Cyanopropan-2-yl dithiobenzoate being generated under these conditions methyl methacrylate (MMA) was added, and its polymerization was initiated with AIBN at 60 °C (Table 1). Figure 1 shows size exclusion chromatography (SEC) traces of samples at different reaction times: the molar mass of poly(methyl methacrylate) (PMMA) evolved linearly with increasing monomer conversion, and PDI values remained below 1.3, indicating a controlled polymerization.

Styrene was also polymerized in the presence of Davy-R reagents (Davy reagents carrying an R alkyl group) in

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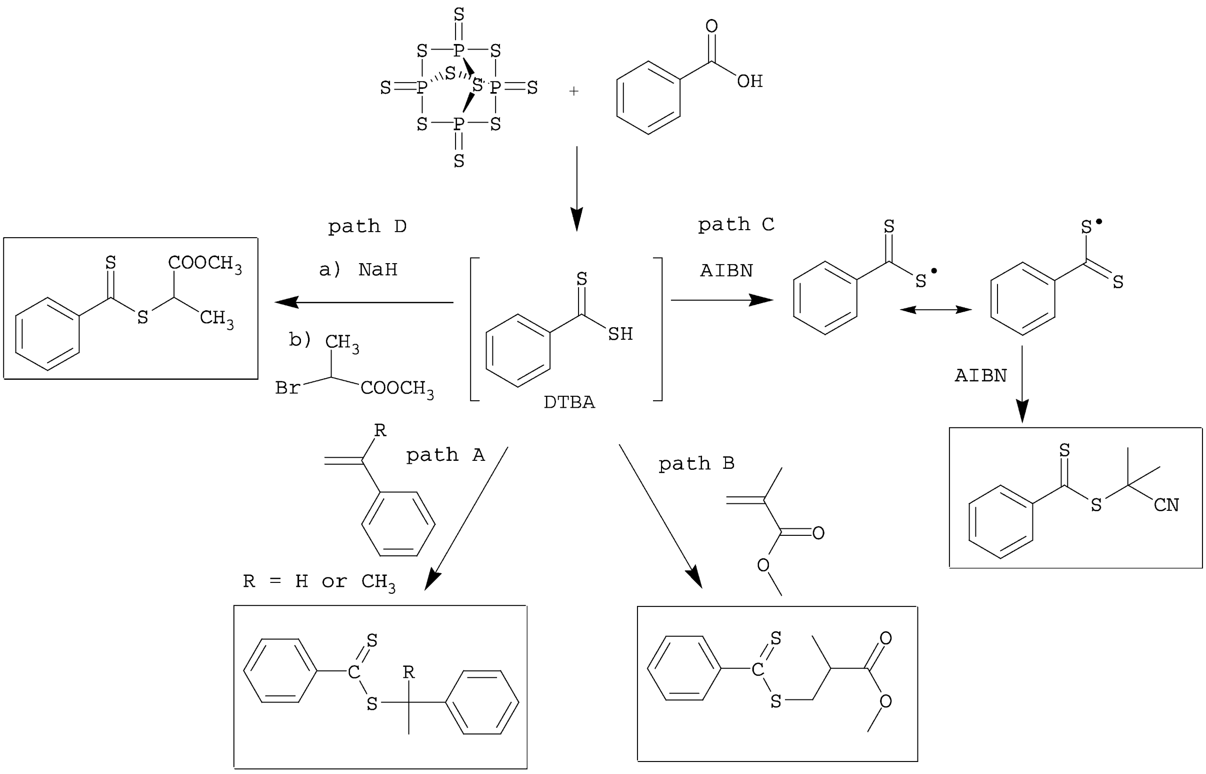


Scheme 2.

Table 1: Polymerization of MMA in toluene at 60 °C with P_4S_{10}, PhCOOH, and AIBN.[a]

t [h]	Conversion [%]	M_n [g mol^{-1}]	PDI
0.62	11.2	6300	1.3
1.25	18.2	9200	1.25
2.25	32.3	14 900	1.2
3.17	42.5	18 700	1.19
17.17	100	42 700	1.25

[a] [PhCOOH] = 0.06 mol L^{-1}; [AIBN] = 0.0135 mol L^{-1}; [MMA] = 5.82 mol L^{-1}.

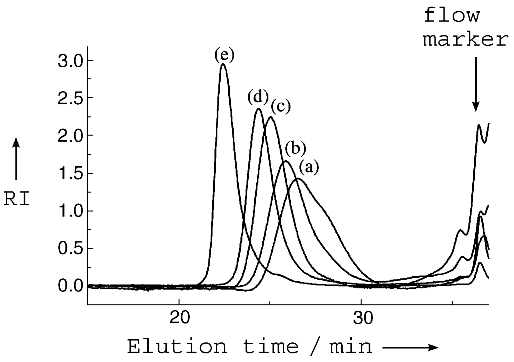
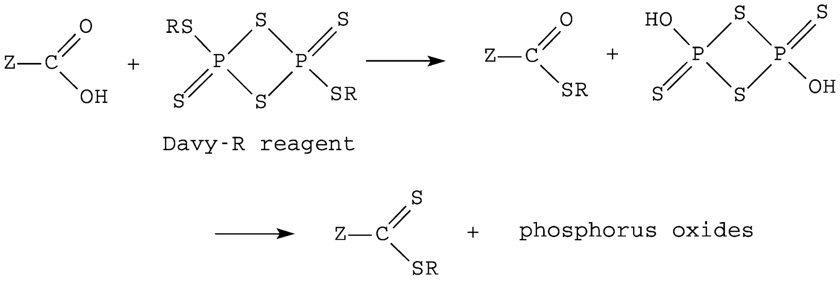


Figure 1. SEC traces (RI) of samples obtained by polymerizing MMA in toluene at 60 °C with P_4S_{10}, AIBN, and PhCOOH, see Table 1; a) $t = 0.62$ h, b $t = 1.25$ h, c) $t = 2.25$ h, d) $t = 3.17$ h, e) $t = 17.17$ h.

conjunction with PhCOOH. It was first verified that the reaction of a Davy-R reagent with PhCOOH effectively yields the dithioester PhC(=S)SR (Scheme 3).[7–11] Afterwards, styrene and AIBN were added to a medium containing benzyl dithiobenzoate formed in situ, and the mixture was heated to 60 °C (Table 2). A continuous increase in molar mass with increasing monomer conversion was observed by SEC. This indicates that methyl, phenyl, and benzyl dithiobenzoates formed in situ controlled the polymerization of styrene. The PDI of the PS samples decreased in the following order: R = benzyl > R = phenyl > R = methyl, which is related to the rate of fragmentation of the homolytic group R.[4] We also noted that the M_n



Scheme 3.

Table 2: Polymerization of styrene in toluene at 60 °C with Davy-R reagents and PhCOOH.

R	t [h]	Conversion [%]	M_n [g mol^{-1}]	PDI
CH_3	17.83	7	2600	1.14
	118	50	15 000	1.72
Ph	44.5	17.5	2450	1.25
	141.5	37.5	2740	1.53
CH_2Ph	7.5	22	1200	1.1
	23	45	4000	1.05

values did not match those expected from the ratio of [monomer] to [PhCOOH] used. This result was attributed to incomplete formation of the dithioester from the reaction of Davy-R reagents with PhCOOH. However, all experiments were reproducible.

Finally, this method was applied to the synthesis of block copolymers. Figure 2 shows the SEC trace of a poly(methyl acrylate) (PMA) precursor synthesized by generating benzyl dithiobenzoate in situ and the subsequently formed PMA-*b*-PS diblock copolymer.

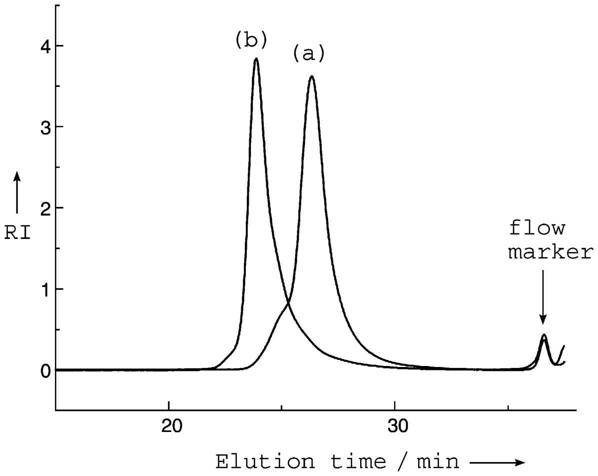


Figure 2. SEC traces (RI) of a PMA obtained by polymerizing MA in toluene at 60 °C with Davy-benzyl reagent and PhCOOH (a) and PMA-*b*-PS diblock copolymer after chain extension (b).

In summary, the use of P_4S_{10} or Davy reagents in conjunction with PhCOOH proved versatile in controlling the free-radical polymerization of styrene and (meth)acrylates under simple conditions. Dithioesters are generated in situ and serve as CTAs in a RAFT process. Dithiobenzoic acid formed by reaction of P_4S_{10} with PhCOOH is the key intermediate in the synthesis of dithioesters. Work is in progress to apply this simple method to the preparation of star polymers.

Experimental Section

AIBN was recrystallized from methanol. P_4S_{10}, Davy-R reagent (R = Me, Ph), benzyl thiol, benzoic acid, and methyl 2-bromopropionate (Aldrich) were used as received. Toluene, styrene, methyl methacrylate, and methyl acrylate (Aldrich) were distilled from CaH_2. The Davy-benzyl reagent was prepared as previously reported in ref. [1617] Polymerization reactions were performed after degassing by freeze–thaw cycles. NMR spectra were recorded on a Bruker AC200 NMR spectrometer. SEC was performed in THF at 25 °C (flow rate 1 mL min^{-1}) on a Varian apparatus equipped with refractive index (Varian)/UV dual detection and fitted with TSK column pack (G3,000HXL, G4,000HXL, G2,000HXL) or on a fast SEC column (PSS SDV linear M 5µ 8 × 300 mm). Calibration was performed with linear PS standards.

Synthesis of cyanoisopropyl dithiobenzoate (Scheme 2, path C): P_4S_{10} (580 mg, 1.3×10^{-3} mol), PhCOOH (670 mg, 5.5×10^{-3} mol), AIBN (2.5 g, 1.5×10^{-2} mol), and toluene (30 mL) were heated at 110 °C for 1 h. The mixture was poured into cyclohexane and the filtrate was purified by chromatography (silica gel in CH_2Cl_2 and alumina with hexane/diethyl ether 9/1). ^1H NMR (200 mHz, $CDCl_3$): $\delta = 1.9$ (6 H, s, $2 \times CH_3$), 7.4 (2 H, dd, *m*-ArH), 7.6 (1 H, dd, *p*-ArH), 7.9 ppm (2 H, d, *o*-ArH); ^{13}C NMR (50 mHz, $CDCl_3$): $\delta = 27$ (CH_3), 42.3 (C(CN)), 120.6 (CN), 127.3, 129.2, 133.5, 145.1 (ArC), 223.75 ppm (C=S); MS: *m/z* (%): 221 (11), 153 (16), 121 (85), 105 (68), 77 (100).

Synthesis of propionyl dithiobenzoate (Scheme 2, Path D): P_4S_{10} (7.3 g, 1.64×10^{-2} mol), PhCOOH (2 g, 1.64×10^{-2} mol), and toluene (30 mL) were heated at 110 °C for 1 h. The mixture was washed with water at pH 10. After washing with diethyl ether, the aqueous phase was reacidified. After addition of acetonitrile, the solution was treated with NaH. Methyl 2-bromopropionate bromide was added to this suspension and the mixture stirred for 20 h at room temperature. After concentration, the solution was washed with water and the product purified by column chromatography on silica gel in CH_2Cl_2/heptane (9/1). ^1H NMR (200 mHz, $CDCl_3$): $\delta = 1.67$ (3 H, d, CH_3), 3.76 (3 H, s, $COOCH_3$), 4.77 (1 H, q, $CSSCHCH_3$), 7.2–8.1 ppm (5 H, m, Ph); ^{13}C NMR (50 mHz, $CDCl_3$): $\delta = 127$–145 (Ar), 224 ppm (C=S); MS: *m/z* (%): 240 (8), 207 (7), 121 (100), 77 (31). Polymerization of MMA with P_4S_{10} and PhCOOH (Table 1): PhCOOH (67 mg, 5.5×10^{-4} mol), P_4S_{10} (58 mg, 1.31×10^{-4} mol), and AIBN (250 mg, 1.52×10^{-3} mol) were stirred at 110 °C in toluene (3 mL) for 1 h. After cooling to 60 °C, MMA (6 mL, 5.24×10^{-2} mol) and AIBN (20 mg, 1.22×10^{-4} mol) were added. The mixture was stirred for 24 h. The product was analyzed by SEC after removal of MMA by evaporation (Table 2).

Synthesis of benzyl dithiobenzoate (Scheme 3) and its use to control the polymerization of styrene (Table 2): Davy-benzyl reagent (370 mg, 8.25×10^{-4} mol), PhCOOH (207 mg, 1.65×10^{-3} mol), and toluene (15 mL) were heated at 110 °C for 1 h. Two-thirds of this mixture was withdrawn for analysis after purification by chromatography on silica gel (CH_2Cl_2). ^1H NMR (200 mHz, $CDCl_3$): $\delta = 4.62$ (2 H, s, $CSS{-}CH_2Ph$), 7.2–8.1 ppm (10 H, m, Ph); ^{13}C NMR (50 mHz, $CDCl_3$): $\delta = 42.88$ (SCH_2Ph), 127–145 (Ar), 224 ppm (C=S); MS: *m/z* (%): 244 (13), 228 (25), 121 (22), 105 (100), 91 (37), 77 (38). The remaining third of the mixture was cooled to 60 °C and then styrene (6 mL, 5.24×10^{-2} mol) and AIBN (17.2 mg, 1.05×10^{-4} mol) were added. The solution was analyzed by SEC after removal of styrene by evaporation.

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