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Rapid Block Copolymer Synthesis by Microwave-Assisted RAFT Polymerization

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ABSTRACT: A single-mode microwave reactor was employed for the synthesis of well-defined homopolymers and block copolymers of acrylamido and acrylate monomers via reversible addition−fragmentation chain transfer (RAFT) polymerization. The rates of polymerization of *N*,*N*-dimethylacrylamide and *N*-isopropylacrylamide were significantly higher than those observed under conventional heating conditions, yet the resulting homopolymers retained thiocarbonylthio end group functionality, as evidenced by efficient extension during block copolymerizations. Moreover, the dramatically enhanced rates of polymerization observed under microwave conditions did not negatively affect molecular weight control during homopolymerization or block copolymerization. In all cases, low polydispersity indices were observed, and the agreement between theoretical and experimental molecular weights was excellent. Rate enhancement may ultimately be the result of thermal effects not easily duplicated under conventional heating conditions. The methods outlined herein permit the total synthesis of block copolymers in a dramatically shortened period of time.

Introduction

Microwave-assisted chemical synthesis is a widely employed technique that leads to enhanced rates, yields, and purities in comparison to reactions conducted with conventional heating.[1−5] Under optimized conditions, reactants directly absorb microwave irradiation, as compared to the typical conventional heating cases (e.g., with an oil bath or heating block) in which energy is transferred, often via solvent, by thermal conduction. Success in the field of small molecule microwave-assisted organic synthesis[6−14] has given rise to growing interest in using microwaves as a heating source for polymerizations and post-polymerization modifications.[15−28] The potential ability to accelerate polymerization reactions while simultaneously reducing the probability of side reactions indicates this method may prove particularly useful during the synthesis of well-defined polymers.

Microwave-assisted conventional radical polymerizations of various monomers, including styrene,[29−33] methyl methacrylate (MMA),[26,32,33] (meth)acrylamides,[34−36] *N*-benzenesulfonamide maleimide,[37] and dialkylfumarates[38] have been widely investigated. However, reports of controlled radical polymerizations (CRP) being conducted under microwave conditions are more sparse,[39−41] and the results often appear inconsistent as a result of widely varying reaction setups. Demonceau et al. reported the atom transfer radical polymerization (ATRP) of MMA at temperatures between 85 and 120 °C in a single-mode microwave reactor.[42] Under conventional microwave conditions, well-defined polymer was obtained; however, when the polymerizations were simultaneously cooled by blowing air over the outside of the reaction vessel during irradiation, a practice employed to allow increased microwave intensity under isothermal conditions, uncontrolled polymerization was observed. Enhanced rates and low polydispersity indices were reported for the ATRP of MMA in a modified domestic microwave oven,[43] while no rate enhancement was observed for a similar polymerization conducted in a single-mode microwave reactor specifically designed for chemical synthesis.[44] Similarly, significant rate enhancements were reported for the nitroxide-mediated polymerization (NMP) of styrene in a multimode microwave reactor,[45] but no appreciable microwave-enhanced acceleration was observed during the NMP of methyl acrylate (MA) and *tert*-butyl acrylate.[46] During the reversible addition−fragmentation chain transfer (RAFT) polymerization of styrene in a multimode modified domestic microwave, Zhu et al. observed a considerable rate enhancement.[47] Perrier and co-workers investigated microwave-enhanced RAFT polymerization of polar and nonpolar monomers, such as MA, MMA, vinyl acetate, and styrene, with and without temperature control in a single-mode microwave reactor.[48,49] In some cases, an extraordinary increase in rate was observed during the polymerization of MA (152%) and MMA (254%). More recently, the microwave-assisted RAFT polymerization of *N*,*N*-diallyldimethylammonium chloride was reported,[50] with high molecular weight polymer being formed during a polymerization that demonstrated a rate enhancement of 520%, as compared to that conducted with conventional heating. Hawker and Stucky et al. reported the microwave-assisted precipitation (co)polymerization of *N*-isopropylacrylamide (NIPAM),[51] and in a recent article, Hoogenboom and Schubert et al. reported the initiator-free RAFT polymerization of MMA in microwave at high temperature.[52]

While there are a few examples of successful homopolymer chain extension during CRP under microwave conditions, block copolymerization has only rarely been reported.[51] As described above, significant rate enhancements were observed in many of the previously reported CRP processes. If the dramatic increase in rates observed for these microwave-assisted polymerizations are the result of increased radical concentrations, a higher

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Table 1. Microwave-Assisted Reversible Addition−Fragmentation Chain Transfer Homopolymerization of *N*,*N*-Dimethylacrylamide (DMA) or *N*-Isopropylacrylamide (NIPAM)

entry	monomer	temp[a] (°C)	heating method[b]	[M]/[CTA]/[I][c]	time[d] (min)	Conv.[e] (%)	$M_{n,th}$[f] (g/mol)	M_n[g] (g/mol)	PDI
A	DMA	70	EMW	[100]/[1]/[0.05]	2	73	7600	7700	1.18
B	DMA	70	EMW	[200]/[1]/[0.05]	5	75	15300	14700	1.20
C	DMA	70	EMW	[400]/[1]/[0.05]	5	52	20900	23800	1.19
D	DMA	70	EMW	[100]/[1]/[0.005]	5	46	5000	5100	1.12
E	DMA	70	MW	[100]/[1]/[0.05]	5	44	4700	5000	1.11
F	DMA	70	MW	[200]/[1]/[0.05]	5	35	7300	9000	1.20
G	DMA	70	CH	[100]/[1]/[0.05]	50	73	7600	9200	1.16
H	DMA	70	CH	[200]/[1]/[0.05]	70	71	14400	14100	1.13
I	DMA	70	CH	[400]/[1]/[0.05]	90	51	20800	21400	1.28
J	DMA	70	CH	[100]/[1]/[0.005]	180	45	4800	4500	1.19
K	NIPAM	60	EMW	[100]/[1]/[0.05]	10	61	7200	6500	1.20
L	NIPAM	60	EMW	[200]/[1]/[0.05]	20	55	12800	11900	1.15
M	NIPAM	60	MW	[100]/[1]/[0.05]	40	52	6200	6000	1.17
N	NIPAM	60	EMW	[200]/[1]/[0.05]	50	54	12000	10800	1.17
O	NIPAM	60	CH	[100]/[1]/[0.05]	420	56	6700	6500	1.17
P	NIPAM	60	CH	[200]/[1]/[0.05]	1440	0			

[a] Programmed temperature for the microwave polymerizations and reaction block temperature for the conventionally heated samples. [b] MW: standard microwave heating; EMW: enhanced microwave heating; CH: conventional heating. [c] Molar ratio of [monomer (M)]/[chain transfer agent (CTA)]/[initiator (I)]. [d] Holding time in microwave reactor at predetermined temperature. [e] Monomer conversion determined by ^{1}H NMR spectroscopy. [f] Theoretical number average molecular weight ($M_{n,th}$). [g] Number average molecular weight (M_n) determined by size exclusion chromatography.

proportion of terminated chains might also be expected. While the homopolymers prepared by microwave-assisted CRP have generally been well-defined with controlled molecular weights, a potential increase in the fraction of dead chains could prevent efficient block copolymer extension in subsequent steps. Therefore, it is important to investigate block copolymer synthesis from homopolymers prepared by microwave heating. Herein, we report the highly accelerated microwave-assisted RAFT synthesis of well-defined homopolymer macro chain transfer agents (macroCTAs) and their subsequent chain extension to form block copolymers.

Experimental Section

Materials. The 2-dodecylsulfanylthiocarbonylsulfanyl-2-methylpropionic acid (DMP) chain transfer agent (CTA) was prepared as previously reported.[53] *N*,*N*-Dimethylacrylamide (Fluka, 98%), MA (Acros Organics, 99%), *n*-butyl acrylate (BA; Fluka, 99+%), and 1,4-dioxane (Alfa Aesar, 99+%) were passed through a small column of basic alumina prior to use. NIPAM (TCI, 98%) was recrystallized three times from hexane. 2,2′-Azobisisobutyronitrile (AIBN, Sigma, 98%) was recrystallized from ethanol. 1,3,5-Trioxane (Acros Organics, 99.5%), *N*,*N*-dimethylformamide (DMF; Aldrich 99.9%), benzene (EMD, 99.8%), hexane (Fisher, 99.9%), tetrahydrofuran (THF; Mallinckrodt, 99%), diethyl ether (Fisher Scientific, 99.9%), and $CDCl_3$ (Cambridge Isotope, 99% D) were used as received. All other reagents were obtained from VWR and used without further purification.

Instruments and Analyses. Microwave-assisted RAFT polymerization was performed in a single-mode microwave reactor (CEM Discover Labmate) equipped with a newly calibrated infrared temperature sensor (Maximum pressure = 250 psi, maximum power = 200 W). The polymerizations were conducted with or without simultaneous cooling by compressed air flow. For the polymerizations conducted with simultaneous cooling, compressed air pressure remained constant at 10 psi. The approximate ramping time varied between 1 and 2 min depending on the temperature setup and the polar nature of the species in the polymerization. The safety release temperature of the instrument was set above the reaction temperature to allow the reaction vials to be removed without a cooling period.

Size exclusion chromatography (SEC) was conducted in 0.05 M LiBr in DMF at 55 °C with a flow rate of 1.0 mL/min (Viscotek VE 2001 GPCmax; columns: guard + two Varian PL_{GEL} Mixed-D columns, molecular weight range $0-400 \times 10^3$ g/mol or ViscoGel I-Series G3000 and G4000 mixed bed columns, molecular weight range $0-60 \times 10^3$ and $0-400 \times 10^3$ g/mol, respectively). Detection consisted of a Viscotek VE 3580 refractive index detector operating at $\lambda = 660$ nm and a Viscotek Model 270 Series Platform, consisting of a laser light scattering detector (operating at 3 mW, $\lambda = 670$ nm with detection angles of 7° and 90°) and a four capillary viscometer. Molecular weight and polydispersity index (PDI) were determined by the triple detection method. ^{1}H NMR spectroscopy was conducted with a Bruker Avance 400 spectrometer operating at 400 MHz. Apparent rate constants of propagation and associated errors were determined by linear regression analysis of the pseudofirst-order rate plots. UV−vis spectroscopy was conducted with a Beckman Coulter DU 800 spectrophotometer.

Microwave RAFT Polymerizations of DMA. An example RAFT polymerization of DMA under microwave heating conditions was as follows. A stock solution was prepared of DMA (2.00 g, 20.2 mmol), DMP (73.6 mg, 0.202 mmol), AIBN (1.7 mg, 0.010 mmol), trioxane (50 mg, internal NMR standard), and benzene (8.0 mL). An aliquot (1 mL) was sealed in a 10 mL glass vial equipped with a magnetic stir bar. The resulting solution was purged with nitrogen for 20 min, the reaction vial was placed in the cavity of the microwave instrument, and the temperature was programmed to 70 °C. After 2 min, the polymerization was quenched by ceasing microwave irradiation, removing the vial from the instrument, rapidly cooling in an ice water bath, and exposing the reaction solution to air. Monomer conversion (73%) was determined by ^{1}H NMR spectroscopy, comparing the area of the trioxane (-CH_2-) signal at $\delta \approx 5$ ppm to one of the monomer vinyl protons ($CH_2=$) at $\delta \approx 5.5$ ppm. Molecular weight ($M_n = 7700$ g/mol, PDI = 1.18) was determined by SEC. Homopolymers employed as macroCTAs were purified by dialysis against deionized water and subsequent lyophilization. Detailed reaction conditions for all homopolymerizations and copolymerizations are given in Table 1.

RAFT Polymerizations of DMA by Conventional Heating. An example RAFT polymerization of DMA by conventional heating was as follows. DMA (1.60 g, 16.1 mmol), DMP (58.9 mg, 0.161 mmol), AIBN (1.3 mg, 0.0079 mmol), trioxane (50 mg, internal NMR standard), and benzene (6.4 mL) were placed in a sealed 20 mL glass vial equipped with a magnetic stir bar. After the contents of the sealed vial were purged with nitrogen for 20 min, the vial was placed in a preheated reaction block at 70 °C. Kinetic samples were removed periodically by nitrogen-purged syringe to determine monomer conversion by ^{1}H NMR spectroscopy and polymer molecular weight by SEC.

Microwave RAFT Polymerizations of NIPAM. An example RAFT polymerization of NIPAM under microwave heating conditions was as follows. A stock solution was prepared with NIPAM (1.38 g, 12.2 mmol), DMP (44.5 mg, 0.122 mmol), AIBN (1 mg, 0.006 mmol), trioxane (50 mg, internal NMR standard), and 1,4-dioxane (664 μL). An aliquot (1 mL) was sealed in a 10 mL glass vial equipped with a magnetic stir bar. The resulting solution was purged with nitrogen for 20 min, the reaction vial was placed in the cavity of the microwave instrument, and the temperature was programmed to 60 °C. After 10 min, the polymerization was quenched by ceasing microwave irradiation, removing the vial from the instrument, rapidly cooling in an ice water bath, and exposing the reaction solution to air. Monomer conversion (61%) was determined by ^{1}H NMR spectroscopy, comparing the area of the trioxane (-CH_2-) signal at $\delta \approx 5$ ppm to one of the monomer vinyl protons (CH_2=) at $\delta \approx 5.5$ ppm. Molecular weight (M_n = 6500 g/mol, PDI = 1.20) was determined by SEC. Homopolymers employed as macroCTAs were purified by precipitating in cold ether, dissolving in water, dialyzing against deionized water, and lyophilizing.

RAFT Polymerizations of NIPAM by Conventional Heating. An example RAFT polymerization of NIPAM by conventional heating was as follows. NIPAM (2.35 g, 20.77 mmol), DMP (75.8 mg, 0.208 mmol), AIBN (1.7 mg, 0.010 mmol), trioxane (50 mg, internal NMR standard), and 1,4-dioxane (794 μL) were placed in a sealed 20 mL glass vial equipped with a magnetic stir bar. After the contents of the sealed vial were purged with nitrogen for 20 min, the vial was placed in a preheated heating block at 60 °C. Kinetic samples were removed periodically by syringe to determine monomer conversion by ^{1}H NMR spectroscopy and molecular weight by SEC.

Microwave Block Copolymerization of PDMA with NIPAM. An example RAFT block copolymerization of PDMA with NIPAM under microwave heating conditions was conducted as follows. PDMA macroCTA (74.5 mg, 0.0118 mmol, M_n = 6300 g/mol, PDI = 1.16), AIBN (0.1 mg, 0.6 μmol), NIPAM (133.3 mg, 1.178 mmol), trioxane (5 mg, internal NMR standard), and 1,4-dioxane (1.0 mL) were sealed in a 10 mL vial equipped with a magnetic stir bar. After purging with nitrogen for 20 min, the sealed vial was placed in the microwave, and the temperature was programmed to 60 °C. After 30 min, the polymerization was quenched by ceasing microwave irradiation, removing the vial from the instrument, rapidly cooling in an ice water bath, and exposing the reaction solution to air. The polymer was isolated by precipitation in cold ether, filtration, and drying under vacuum. Monomer conversion (71%) was determined by ^{1}H NMR spectroscopy, comparing the area of the trioxane (-CH_2-) signal at $\delta \approx 5$ ppm to one of the monomer vinyl protons (CH_2=) at $\delta \approx 5.5$ ppm. Molecular weight (12500 g/mol, PDI = 1.17) was determined by SEC.

Microwave Block Copolymerizations of PDMA with MA and BA. RAFT block copolymerizations of PDMA with MA and BA were conducted in a manner similar to that described above for the synthesis of PDMA-*b*-PNIPAM, except PDMA-*b*-poly(*n*-butyl acrylate) (PDMA-*b*-PBA) was isolated by precipitation in cold hexane, filtration, and drying under vacuum. Molecular weights of the purified PDMA-*b*-poly(methyl acrylate) (PDMA-*b*-PMA; M_n = 9200 g/mol; PDI = 1.2) and PDMA-*b*-PBA (M_n = 14900 g/mol; PDI = 1.2) were determined by SEC.

Microwave Block Copolymerization of PNIPAM with DMA. An example RAFT block copolymerization of PNIPAM with DMA under microwave heating conditions was as follows. PNIPAM macroCTA (68.4 mg, 0.00980 mmol, M_n = 7000 g/mol, PDI = 1.18), AIBN (0.016 mg, 0.097 μmol), DMA (60.5 mg, 0.610 mmol), trioxane (5 mg, internal NMR standard), and 1,4-dioxane (1.0 mL) were sealed in a 10 mL vial equipped with a magnetic stir bar. After purging with nitrogen for 20 min, the sealed vial was placed in the microwave, and the temperature was programmed to 60 °C. After 15 min, the polymerization was quenched by ceasing microwave irradiation, removing the vial from the instrument, rapidly cooling in an ice water bath, and exposing the reaction solution to air. Monomer conversion (55%) was determined by ^{1}H NMR spectroscopy, comparing the area of the trioxane (-CH_2-) signal at $\delta \approx 5$ ppm to one of the monomer vinyl protons (CH_2=) at $\delta \approx 5.5$ ppm. The polymer was isolated by precipitation in cold ether, filtration, and drying under vacuum. Molecular weight (12500 g/mol, PDI = 1.20) was determined by SEC.

Microwave Block Copolymerization of PNIPAM with MA and BA. RAFT block copolymerizations of PNIPAM with MA and BA were conducted in a manner similar to that described above for the synthesis of PNIPAM-*b*-PDMA, except PNIPAM-*b*-PBA was isolated by precipitation in cold hexane, filtration, and drying under vacuum. Molecular weights of the purified PNIPAM-*b*-PMA (12200 g/mol; PDI = 1.17) and PNIPAM-*b*-PBA (M_n = 15500 g/mol; PDI = 1.18) were determined by SEC.

Results and Discussion

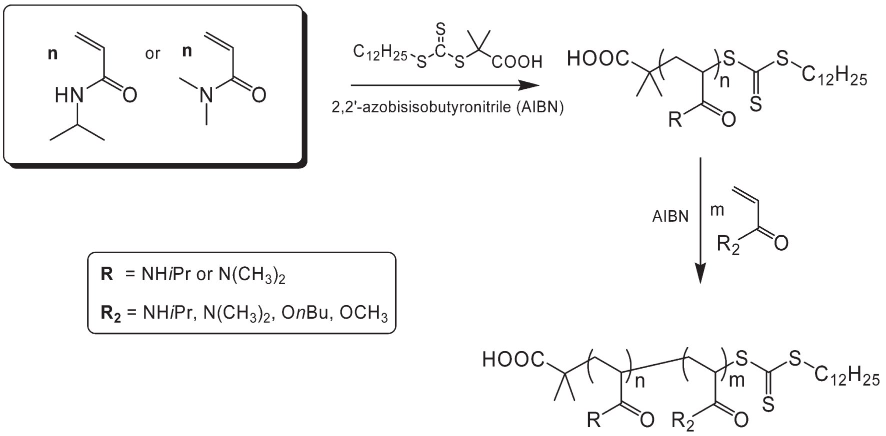
While there have been several reports concerning the microwave-assisted polymerization of styrenic and (meth)acrylate monomers, there has been significantly less attention paid to acrylamido monomers. Our preliminary studies focused on homopolymerizations of DMA and NIPAM, to investigate the effects of heating method, polymerization stoichiometry, and solvent polarity. The resulting homopolymer macroCTAs were subsequently extended by copolymerization with a second monomer to provide accelerated access to block copolymers and to indirectly provide information regarding chain end retention during microwave-assisted CRP.

Microwave-Assisted Homopolymerization of DMA or NIPAM. DMA or NIPAM was polymerized with DMP as the CTA and AIBN as the initiator (Scheme 1). Polymerizations of DMA were conducted at a programmed temperature of 70 °C in benzene with a monomer concentration of 2 M. While polymerizations with these conditions led to well-defined polymers with controlled molecular weight, polymerizations in DMF, a more highly microwave absorbing solvent, led to broad molecular weight distributions and significant chain end loss, potentially the result of unintentionally high initial temperatures in the reaction medium leading to chain transfer or other side reactions during polymerization. Greiner and co-workers reported similar results when DMF was used as the solvent for the microwave-assisted conventional radical (co)polymerization of styrene and MMA.[32,33] Polymerizations of NIPAM were most controlled at a programmed temperature of 60 °C in 1,4-dioxane with a monomer concentration of 1.5 M.

Two different microwave conditions were initially considered. Many microwave polymerization instruments allow the reaction contents to be simultaneously cooled during microwave heating by the controlled application of a compressed air stream over the outside of the reaction vessel during irradiation. This enhanced microwave process is a common practice that allows increased microwave power to be applied under what are thought to be isothermal conditions.[13] Hereafter, the microwave method accompanied by simultaneous cooling will be referred to as the enhanced microwave (EMW) approach, and the microwave method without simultaneous cooling will be denoted as the standard microwave (MW) approach.[42] The initial microwave homopolymerizations of DMA were investigated under both EMW and MW conditions.

During the course of the polymerization, an IR sensor within the instrument was used to monitor the temperature

Scheme 1. Microwave-Assisted Reversible Addition−Fragmentation Chain Transfer Homopolymerization of *N*,*N*-Dimethylacrylamide (DMA) or *N*-Isopropylacrylamide (NIPAM) and Subsequent Block Copolymerization with NIPAM, DMA, Butyl Acrylate, or Methyl Acrylate



of the microwave vial and to serve as a thermostat to meter the microwave power such that a near constant apparent temperature was maintained. To compare the results obtained under microwave conditions, our goal was to conduct polymerizations at the same temperature with conventional heating using a heating block or oil bath. When the conditions employed here were used, and assuming the IR temperature sensor was reasonably accurate, the microwave reactions were significantly faster than those conducted with conventional heating. However, there has been some debate regarding the accuracy of the instrument IR sensor during reactions that employ the EMW approach. An accurate comparison of rates with conventional heating requires the polymerization temperature to be constant in both reaction setups. Therefore, several model experiments were conducted to investigate the accuracy of the IR sensor by measuring the actual internal temperature of the polymerization solution (Supporting Information). Potentially due to the rapid onset and exothermic nature of the polymerization, the temperature within the microwave vial was indeed initially higher than the programmed temperature, reaching 82 °C after approximately 2 min before gradually dropping to the programmed temperature of 70 ± 2 °C after a period of approximately 4−6 min (Supporting Information). This initial increase in temperature under microwave conditions is relatively common and has been reported by several others.[48,54] While the brief periods of higher polymerization temperature certainly contributed to increased rates, it seems unlikely rate acceleration under microwave conditions can be solely explained by this initial exothermicity, especially given that the accelerations in rate were so significant (vide infra). In fact, model polymerizations conducted with conventional heating at a constant temperature of 85 °C were still two times slower and, incidentally, less controlled than the microwave polymerizations programmed for 70 °C (Figure S2, Supporting Information). The explanations for rate enhancement remain debatable and may ultimately be the result of thermal effects not easily duplicated under conventional heating conditions.

Homopolymerizations of DMA were conducted with ratios of [DMA]/[CTA]/[initiator] = 100/1/0.05 and 200/1/0.05 with conventional, MW, and EMW heating. In all cases, the rates of the polymerizations heated by microwave were significantly increased, as compared to polymerizations conducted with conventional heating. For instance, the polymerization with [DMA]/[CTA]/[initiator] = 100/1/0.05 showed no monomer conversion after 30 min with conventional heating, but a conversion of 73% was obtained in 2 min with EMW heating (Table 1, entry A). A similar conversion with conventional heating required 50 min (Table 1, entry G). The acceleration observed during the microwave reactions was diminished when the simultaneous cooling feature was not employed, but the polymerizations remained faster than those conducted with conventional heating, with 44% conversion being obtained in 5 min via the MW approach (Table 1, entry E). The same general trend in polymerization rates was observed for polymerizations that targeted higher molecular weights ([DMA]/[CTA]/[initiator] = 200/1/0.05).

Induction periods were observed for the conventionally heated RAFT polymerizations, but the microwave reactions began immediately with high levels of monomer conversion being reached in a few short minutes. This observation is potentially explained by the rapid heating profile and higher-than-programmed temperatures observed at early stages in the microwave polymerizations (Supporting Information). The resulting increase in the initial rate of radical generation could cause rapid initialization and/or faster consumption of any impurities, thereby leading to an earlier onset of polymerization. The apparent rate constants of propagation (k_p^{app}), obtained from the linear regression slope of the pseudo-first-order kinetic plots (Figure 1A,C), demonstrated that the rate of polymerization remained significantly faster during the microwave reactions. The slopes of these kinetic plots were initially constant, though some curvature was apparent at higher conversions, likely a result of termination events and/or slight reductions in temperature as the polymerizations proceeded. Table 2 contains a list of k_p^{app} values obtained for polymerizations conducted with a variety of stoichiometric ratios and heating conditions. With [DMA]/[CTA]/[initiator] = 100/1/0.05, the relative values of k_p^{app} for the polymerizations with conventional, MW, and EMW heating were 1 to 3 to 16.5, respectively. Therefore, even while ignoring the induction period observed with conventional heating, the rates of polymerization with microwave heating were up to 1550% faster. Similar accelerations were observed for the polymerizations with [DMA]/[CTA]/[initiator] = 200/1/0.05. Homopolymerizations of NIPAM demonstrated comparable microwave-enhanced rates at [NIPAM]/[CTA]/[initiator] = 100/1/0.05 and 200/1/0.05 (Table 1, Figure 2). Similar to the results obtained with DMA, the polymerization with [NIPAM]/[CTA]/[initiator] = 100/1/0.05 led to relative values of k_p^{app} of 1 to 3 to 14 for the polymerizations with conventional, MW, and EMW heating, respectively.

Regardless of the heating method employed, the level of control achieved during the polymerization was excellent. In

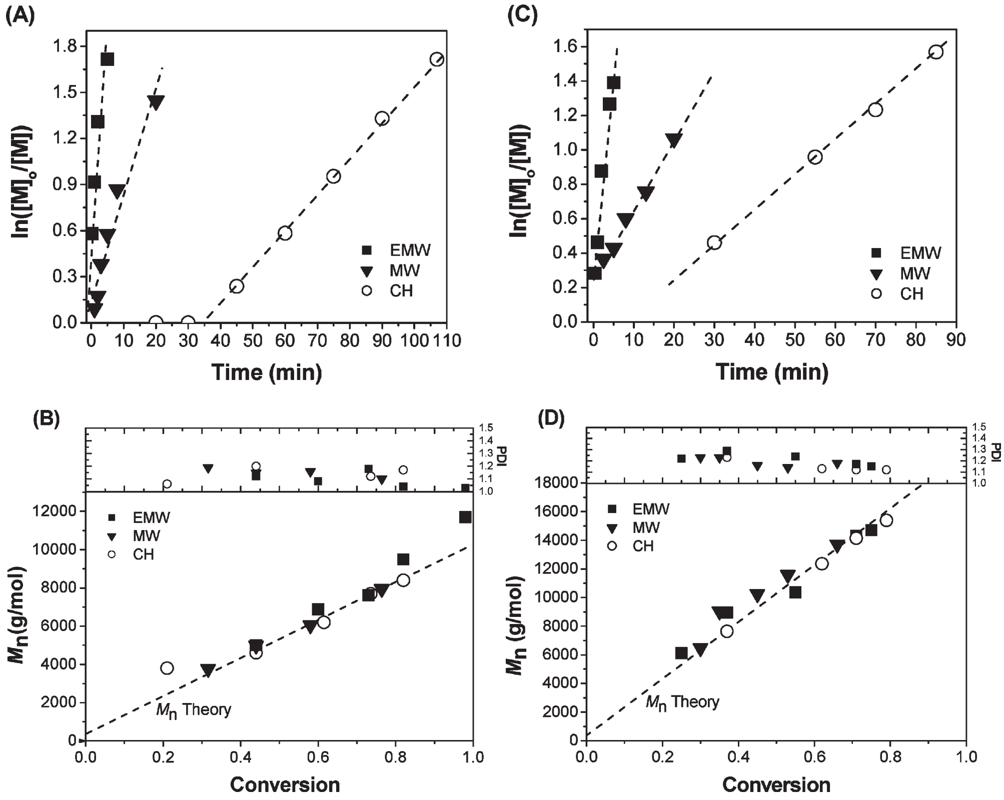


Figure 1. (A) Pseudo-first-order kinetic plot and (B) number average molecular weight (M_n) vs conversion for reversible addition−fragmentation chain transfer (RAFT) polymerization of *N*,*N*-dimethylacrylamide (DMA) with molar ratios of [monomer (M)]/[chain transfer agent (CTA)]/[initiator (I)] = 100/1/0.05; (C) Pseudo-first-order kinetic plot and (D) number average molecular weight (M_n) vs conversion for RAFT polymerization of DMA with molar ratios of [M]/[CTA]/[I] = 200/1/0.05. MW: standard microwave heating; EMW: enhanced microwave heating; CH: conventional heating.

all reactions, the pseudo-first-order rate plots remained relatively linear, with only a slight amount of deviation being observed at high conversion. Similarly, the agreement between theoretical and experimental molecular weights was consistently good, and the polydispersity index of the polymers obtained during the polymerizations of DMA and NIPAM were consistently low (Table 1, Figures 1 and 2). Representative SEC traces from the polymerization of each monomer are shown in Figure 3. In all cases, molecular weight distributions were narrow and unimodal. Because polymerization control was not sacrificed while achieving dramatically accelerated rates of polymerization, the EMW approach was employed for the remainder of the studies discussed below.

A wide variety of stoichiometric conditions ([monomer]/[CTA]/[initiator]) were considered for the homopolymerizations of both DMA and NIPAM. In all cases, polymerization rates were high, and the level of control achieved was similar to that typically observed for conventionally heated polymerizations (Figures S3 and S4, Supporting Information). For instance, even when a higher molecular weight polymer was targeted ([DMA]/[CTA]/[initiator] = 400/1/0.05), PDMA with M_n = 37400 g/mol ($M_{n,theory}$ = 33800 g/mol) and PDI = 1.10 were obtained at 80% conversion in just 10 min. Additionally, successful and sufficiently fast polymerizations were possible with extremely low [CTA]/[initiator] ratios. While a function of many factors (e.g., polymerization temperature, initiator half-life, etc.), typical [CTA]/[initiator] ratios for RAFT are on the order of 2/1, 5/1, 20/1, and so on. Employing the EMW method, the RAFT of DMA with [CTA]/[initiator] = 200/1 ([DMA]/[CTA]/[initiator] = 100/1/0.005) led to 45% monomer conversion in 5 min and PDMA with M_n = 5100 g/mol ($M_{n,theory}$ = 5000 g/mol) and a PDI = 1.12 (Table 1, entry D). With conventional heating, the first signs of polymer were only observed after a 2 h induction period, and 3 h were required to reach a similar level of conversion (Table 1, entry J).

Table 2. Apparent Rate Constants of Propagation (k_p^{app}) as a Function of Heating Method

monomer	[M]/[CTA]/[I][a]	Temp.[b] (°C)	$k_p^{app} \times 10^3$ s^{-1} EMW	MW	CH
DMA	[100]/[1]/[0.05]	70	6.6 ± 0.01	1.2 ± 0.1	0.4 ± 0.01
DMA	[200]/[1]/[0.05]	70	4.0 ± 0.04	0.7 ± 0.01	0.3 ± 0.47
DMA	[400]/[1]/[0.05]	70	1.2 ± 0.03		0.2 ± 0.01
DMA	[100]/[1]/[0.005]	70	1.1 ± 0.02		0.1 ± 0.01
NIPAM	[100]/[1]/[0.05]	60	1.4 ± 0.16	0.3 ± 0.02	0.1 ± 0.01
NIPAM	[200]/[1]/[0.05]	60	0.6 ± 0.05	0.2 ± 0.02	

[a] Molar ratio of [monomer (M)]/[chain transfer agent (CTA)]/[initiator (I)]. EMW: enhanced microwave heating; MW: standard microwave heating; CH: conventional heating. [b] Programmed temperature of the microwave instrument.

Microwave-Assisted Block Copolymerization. As described above, the microwave-assisted homopolymers prepared by RAFT were well-defined and had controlled molecular weights. However, end group fidelity is also an important aspect to be considered for any CRP process. If microwave-assisted polymerizations are accelerated but the resulting products are incapable of chain extension, a significant limitation in this approach will be realized. Efficient retention of the ω-trithiocarbonate moiety during homopolymerization could be confirmed by UV−vis spectroscopy (Supporting Information), but to further investigate end group fidelity, the homopolymers prepared under microwave heating conditions were employed as macroCTAs for subsequent block copolymerization. The polymerization of

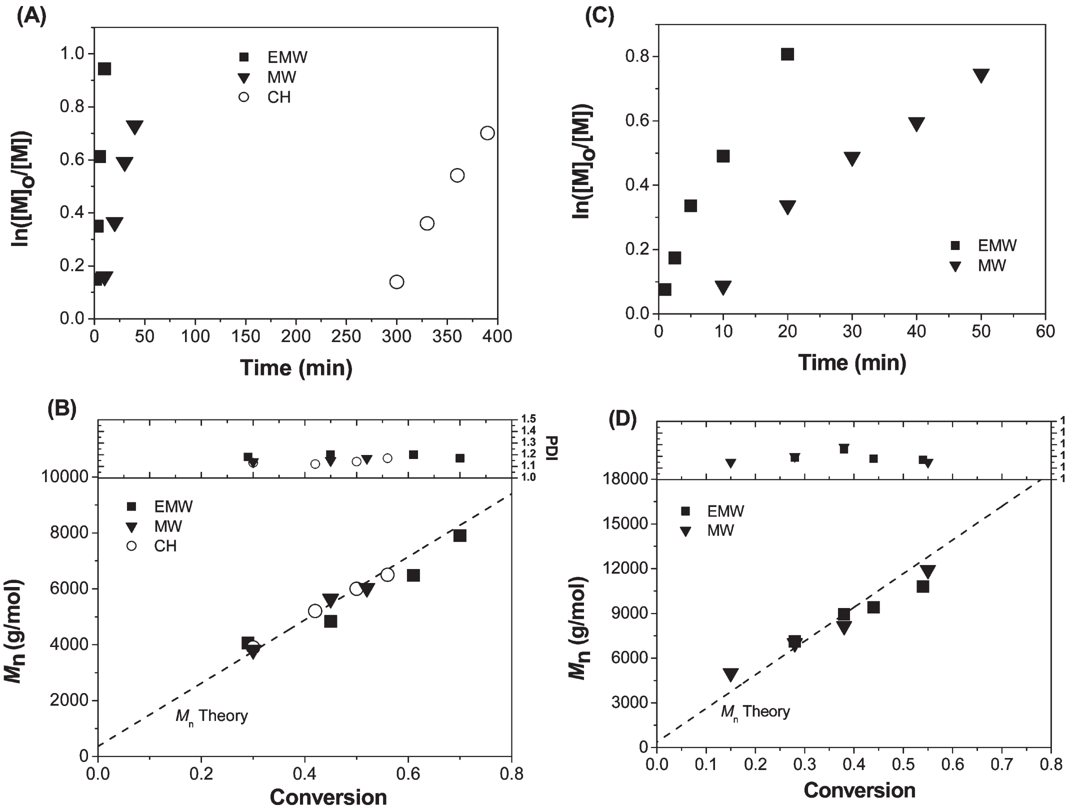


Figure 2. (A) Pseudo-first-order kinetic plot and (B) number average molecular weight (M_n) vs conversion for reversible addition–fragmentation chain transfer (RAFT) polymerization of *N*-isopropylacrylamide (NIPAM) with molar ratios of [monomer (M)]/[chain transfer agent (CTA)]/[initiator (I)] = 100/1/0.05; (C) Pseudo-first-order kinetic plot and (D) number average molecular weight (M_n) vs conversion for RAFT polymerization of NIPAM with molar ratios of monomer [M]/[CTA]/[I] = 200/1/0.05. MW: standard microwave heating; EMW: enhanced microwave heating; CH: conventional heating.

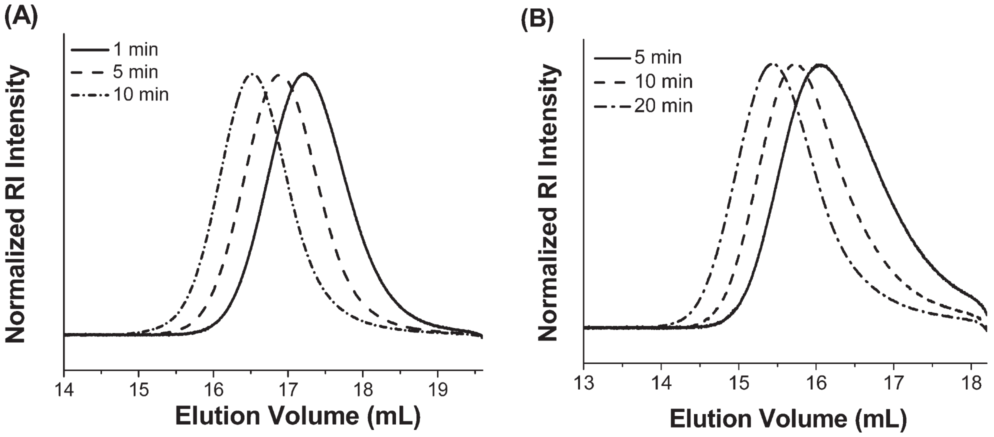


Figure 3. SEC traces for the microwave-assisted reversible addition–fragmentation chain transfer (RAFT) polymerization of (A) *N*,*N*-dimethylacrylamide (DMA) at 70 °C with [monomer (M)]/[chain transfer agent (CTA)]/[initiator (I)] = 100/1/0.05 (Table 1, entry A) and (B) *N*-isopropylacrylamide (NIPAM) at 60 °C with [M]/[CTA]/[I] = 200/1/0.05 (Table 1, entry L).

the second monomer was also achieved via microwave heating, which allowed significantly accelerated access to block copolymers. To avoid inefficient mixing that may result from the viscosity of the initial macroCTA polymerization solutions, reduced concentrations of monomer, CTA, and initiator were employed during the syntheses of the second blocks. As is commonly the practice when preparing block copolymers from homopolymers made under conventional heating conditions, macroCTAs prepared in homopolymerizations that reached relatively moderate monomer conversion (< 70%) were used.

Extension of PDMA macroCTAs with a variety of acrylamido and acrylate monomers (Scheme 1) was rapid and resulted in well-defined block copolymers with low PDI and unimodal molecular weight distributions. In all cases, excellent blocking efficiency was observed with no noticeable homopolymer impurity being visible in the SEC traces (Figure 4). For instance, when PDMA (M_n = 6300 g/mol, PDI = 1.16) prepared in just 1 min (56% conversion) under microwave conditions was employed as a macroCTA for the polymerization of NIPAM ([NIPAM]/[PDMA macroCTA]/[initiator] = [100]/[1]/[0.05]), 71% monomer

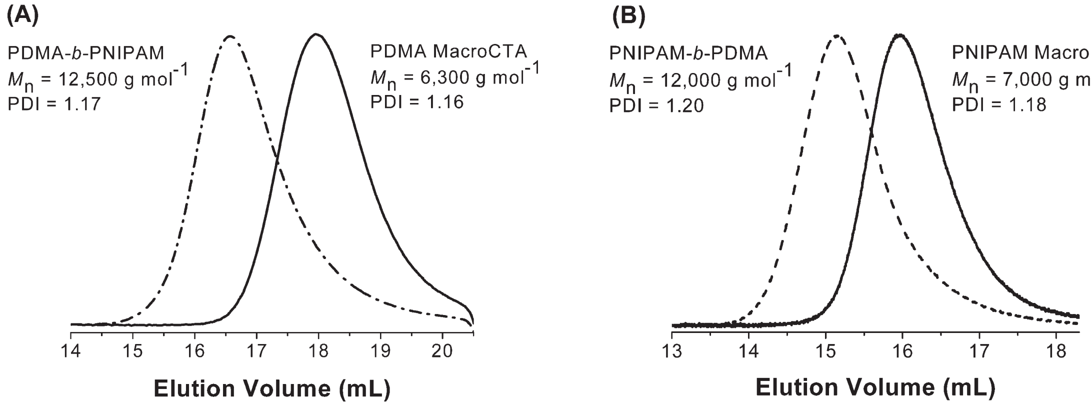


Figure 4. Size exclusion chromatography traces for macro-chain transfer agents (macroCTA) and block copolymers prepared by the enhanced microwave (EMW) approach. (A) Poly(*N*,*N*-dimethylacrylamide) (PDMA) macroCTA and PDMA-*b*-poly(*N*-isopropylacrylamide) (PDMA-*b*-PNIPAM) block copolymer; (B) Poly(*N*-isopropylacrylamide) (PNIPAM) macroCTA and PNIPAM-*b*-PDMA block copolymer.

Table 3. Block Copolymerizations with Poly(*N*,*N*-dimethylacrylamide) and Poly(*N*-isopropylacrylamide) Macro-Chain Transfer Agents under Microwave Heating Conditions

entry	block copolymer	[M]/[MacroCTA]/[I][a]	temp.[b] (°C)	time[c] (min)	conv.[d] (%)	$M_{n,theory}$[e] (g/mol)	M_n[f] (g/mol)	PDI[f]
O	PDMA-*b*-PMA	[100]/[1]/[0.05]	70	60	43	9400	9200	1.20
P	PDMA-*b*-PBA	[100]/[1]/[0.05]	70	45	61	14100	14900	1.20
Q	PDMA-*b*-PNIPAM	[100]/[1]/[0.05]	60	30	71	14300	12500	1.17
R	PNIPAM-*b*-PMA	[60]/[1]/[0.04]	70	90	60	9900	12200	1.17
S	PNIPAM-*b*-PBA	[100]/[1]/[0.05]	70	45	47	13500	15500	1.18
T	PNIPAM-*b*-PDMA	[62]/[1]/[0.01]	60	15	55	10400	12000	1.20

[a] Molar ratio of [monomer (M)]/[macro chain transfer agent (macroCTA)]/[initiator (I)]. [b] Programmed temperature of the microwave instrument. [c] Holding time in microwave reactor at predetermined temperature. [d] Determined by ^{1}H NMR spectroscopy. [e] Theoretical number average molecular weight. [f] Number average molecular weight determined by size exclusion chromatography. PDMA: poly(*N*,*N*-dimethylacrylamide); PMA: poly(methyl acrylate); PBA: poly(*n*-butyl acrylate); PNIPAM: poly(*N*-isopropylacrylamide).

conversion was obtained in 30 min, resulting in polymer with M_n = 12500 g/mol (PDI = 1.17; $M_{n,theory}$ = 14300 g/mol; Table 3, entry Q; and Figure 4A). Similarly, well-defined block copolymer formation was successful during the extension of PDMA with MA and BA. PNIPAM macroCTAs prepared by the EMW approach were also successfully utilized to copolymerize DMA, MA, and BA. For instance, a PNIPAM homopolymer (M_n = 7000 g/mol, PDI = 1.18) prepared in just 12 min (68% conversion) under microwave conditions was employed as a macroCTA for the polymerization of DMA ([DMA]/[PNIPAM macroCTA]/[initiator] = [62]/[1]/[0.01]). In just 15 min (55% conversion), PNIPAM-*b*-PDMA block copolymer with M_n = 12000 g/mol (PDI = 1.20; $M_{n,theory}$ = 10400 g/mol) (Table 3, entry T) was prepared with good blocking efficiency being observed by SEC analysis (Figure 4B).

Conclusions

RAFT polymerization conducted via microwave heating resulted in dramatically enhanced rates. Despite the rapidity with which homopolymers can be prepared, a high degree of end group fidelity was demonstrated by successfully employing the homopolymers as macroCTAs for subsequent block copolymerizations. The ability for complete reaction preparation, synthesis, and purification of block copolymers in just a few hours is undoubtedly an attractive concept. Despite the large body of literature describing increased yields and rates for microwave-assisted chemical reactions, there is still significant debate regarding the explanation for the observed kinetic enhancement. If it is indeed true that the rate acceleration observed during microwave-assisted RAFT is purely a result of thermal effects (higher-than-expected temperatures), the results reported here may indicate that conventionally heated RAFT polymerizations can be conducted at temperatures much higher than generally employed. However, it should be noted that our initial attempts at mimicking microwave RAFT polymerizations by conventional heating at elevated temperatures were largely unsuccessful and generally resulted in slower reactions and reduced molecular weight control. Regardless, an important conclusion of these results is that microwave heating can be used to prepare well-defined block copolymers by RAFT polymerization in a dramatically shortened period of time. This suggests it might be possible to more rapidly synthesize and screen block copolymers for a variety of materials applications. Additionally, many applications benefit from the wide variety of reactions that can be exploited to modify or functionalize the inherent sulfur-containing end groups derived from RAFT. The fact that homopolymers prepared by microwave-assisted RAFT can be successfully extended during block copolymerization suggests that microwave heating is an excellent method to rapidly prepare well-defined polymers with retained end group functionality that permits subsequent surface immobilization, nanoparticle stabilization, bioconjugation, and other end group modifications.

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

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