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RAFT cryopolymerizations of acrylamides and acrylates in dioxane at −5 °C

Xiao-Li Sun, Wei-Dong He*, Ting-Ting Pan, Zong-Lei Ding, Yu-Juan Zhang

Department of Polymer Science and Engineering, CAS Key Laboratory of Soft Matter Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China

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ABSTRACT

Reversible addition-fragmentation chain transfer (RAFT) cryopolymerizations of acrylamides and acrylates were successfully carried out at −5 °C with cumene hydroperoxide/ascorbic acid as redox initiation couple and 2-dodecylsulfanyl- thiocarbonylsulfanyl-2-methylpropinoic acid as chain transfer agent. The cryopolymerization features of *N*,*N*-dimethylacrylamide (DMA) and *tert*-butyl acrylate (*t*BA) were investigated in view of kinetics, molecular weight and its distribution by proton nuclear magnetic resonance analysis and gel permeation chromatography. Furthermore, sequential block cryopolymerizations of *N*-isopropylacrylamide were performed with the obtained trithiocarbonate- functionalized PDMA or PtBA as macro-CTA and the corresponding block polymers were obtained. All the results demonstrated that these cryopolymerizations bear all the characteristics of controlled/living radical polymerizations.

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1. Introduction

Cryopolymerization is a polymerization technique performed in the moderately frozen solution of monomers at the temperature below the freezing point of mixture [1]. The use of cryopolymerization went back to the 1960s when they were proposed to be promising for the formation of macroporous gels (so-called cryogels) [2–4]. Cryogels possess the interconnected macropores with large size, smooth pore surface and spongy-like morphology [5]. It makes cryogels promising materials used as chromatographic matrices and carriers for different molecules, particles and cells [6,7].

Cryopolymerization also has other advantages, such as easy preparation of polymers with high molecular weight, reduction of side reactions, easy control of polymerization and direct experimental proof of the transient radical intermediates [8,9]. However, as a significant technology, cryopolymerization was rarely reported. In 1983, Lozinsky et al. first demonstrated the chemically-initiated cryopolymerization of unsaturated monomers in frozen solutions [10]. Bakhmutov et al. investigated the formation of polyacrylamide cryogels using *in situ* ^{1}H and ^{2}H NMR spectroscopy, and evidently proved that the polymerization indeed proceeded mainly in the unfrozen liquid microphase of the frozen systems [11]. We also reported one-step synthesis of poly(styrene-*b*-*N*-isopropylacryamide) via interfacial-initiated microemulsion polymerization in frozen state [12]. Generally, the early research had virtually poor continuation.

In the past decade, there has been a rapid progress in controlled/living radical polymerization [13–16]. Among them, reversible addition-fragmentation chain transfer (RAFT) polymerization is arguably the most versatile since it can be adapted to the widest range of monomers under mild reaction conditions [17–19], and has become a powerful technique for the synthesis of well-defined (co)polymers with presuming structures and chain architectures [20–23]. Recently, we performed successfully RAFT cryopolymerizations of water-soluble monomers in their aqueous solution at −15 °C and revealed their well-controlled features [24]. But the number of water-soluble monomers is limited.

In this paper, we extended RAFT cryopolymerizations in organic media and investigated RAFT cryopolymerizations of *N*,*N*-dimethylacrylamide and *tert*-butyl acrylate in dioxane at −5 °C in view of the control features of those cryopolymerizations. As far as our knowledge, RAFT cryopolymerization has never been reported by others. RAFT cryopolymerization has the same virtues as common radical cryopolymerization and RAFT polymerization. In addition, RAFT cryopolymerization further favors the synthesis of well-defined thermo-unstable polymers or polymers from thermo-degradable monomers without protecting chemistry. Thus, RAFT cryopolymerization is promising and attractive from both academic and industrial standpoints.

2. Experimental section

2.1. Materials

N,*N*-Dimethylacrylamide (DMA, 99%, Aldrich) was passed through basic alumina column, and then distilled under vacuum

* Corresponding author. Tel.: +86 551 3600153.
E-mail address: wdhe@ustc.edu.cn (W.-D. He).

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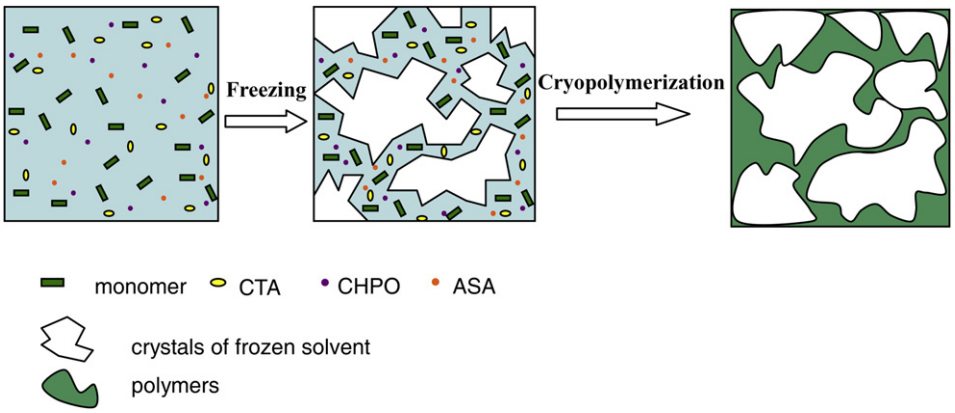

Scheme 1. The process of RAFT cyropolymerization.

over CaH_2 prior to use. *tert*-Butyl acrylate (tBA, Aldrich), *n*-butyl acrylate (nBA) and methyl acrylate (MA) were washed with NaOH aqueous solution, dried over anhydrous $MgSO_4$, distilled under vacuum and stored at −20 °C before use. *N*-Isopropylacrylamide (NIPAM, 99%, Acros) was purified by recrystallization from a benzene/*n*-hexane mixture (65/35 v/v). Cumene hydroperoxide (CHPO, 80%, Alfa Aesar) and ascorbic acid (ASA, 99%) were used without further purification. 1,4-Dioxane was dried over KOH and distilled over benzophenone-sodium prior to use. All un-specified reagents were purchased from Shanghai Chemical Reagent Co. (China). 2-Dodecylsulfanyl-thiocarbonylsulfanyl-2-methylpropinoic acid (DMP) was synthesized and purified as described before [25].

2.2. RAFT Cryopolymerizations of DMA and tBA with DMP as CTAs

DMA (0.495 g, 5 mmol), DMP (18.2 mg, 0.05 mmol), ASA (17.6 mg, 0.1 mmol) and dioxane (5.0 mL) were added into a 25-mL, round-bottom flask equipped with a magnetic stirring bar. Another portion of dioxane was added until the total solution volume was 9.0 mL. The flask was sealed with a rubber septum, and the mixture was purged with nitrogen for 30 min at 10 °C. A dioxane solution of CHPO (1.0 mL, 50 mM) was injected into the reaction mixture. The flask was subsequently kept in the chamber of a cryoreactor (DHJF-4002, Greatwall Scientific Industry & Trade Co. Lt., China) at −5 °C. The polymerization was stopped by rapid cooling in liquid nitrogen at fixed duration. The reaction mixture was precipitated in a large excess of diethyl ether, followed by filtration. The resulting product was redissolved in deionized water, dialyzed against water (molecular weight cutoff of the dialyzing membrane is 500) and subsequent lyophilized in a freeze drier (SIMENS FD5-3, Germany) for 48 h to yield Poly(*N*,*N*-dimethylacryamide) (PDMA) as pale yellow powder. Monomer conversion (*Con*) was determined gravimetrically. The chemical composition and molecular weight were determined by proton nuclear magnetic resonance (^{1}H NMR) spectroscopy and gel permeation chromatography (GPC).

A similar approach has been adopted for the RAFT cryopolymerization of tBA. After the polymerization was stopped, the reaction mixture was precipitated in a large excess of methanol/H_2O (2/1, v/v) at −20 °C, followed by the purification of further precipitation and dryness under vacuum at room temperature.

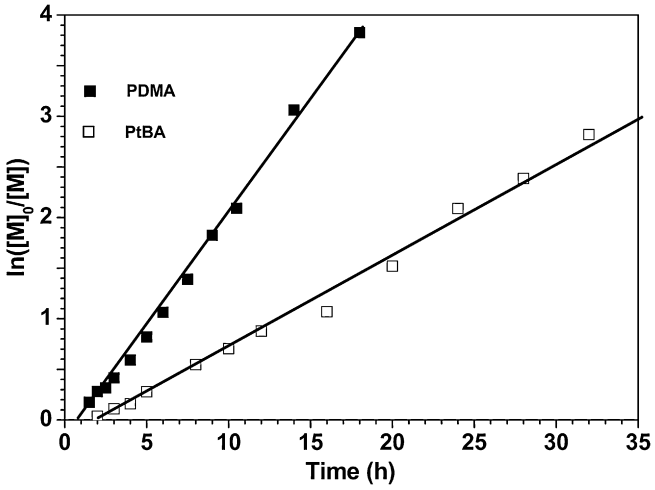

Fig. 1. The kinetic plots for RAFT cryopolymerizations of DMA (■) and tBA(□) using CHPO/ASA as the redox initiators and DMP as the CTA at −5 °C.

2.3. Block RAFT Cryopolymerizations of NIPAM with Macro-CTAs

Trithiocarbonate-functionalized PDMA ($M_{n,NMR}$ = 7100, PDI = 1.09) and poly(*tert*-butyl acrylate) (PtBA) ($M_{n,NMR}$ = 3100, PDI = 1.04) macro-CTAs were used for the introduction of new NIPAM block. The polymerizations were conducted directly in dioxane at an initial monomer concentration of 0.5 M at −5 °C with CHPO/ASA as the initiator. The $[CTA]_0$:$[CHPO]_0$:$[ASA]_0$:$[NIPAM]_0$ ratio was maintained at 1:1:2:100. The polymerizations were allowed to proceed for the selected duration before being quenching in liquid nitrogen. The solvent was removed under vacuum and the obtained mixtures were dissolved in tetrahydrofuran. After filtration, the products were purified by dialysis against deionized water using a dialyzing membrane (molecular weight cutoff, 500) and isolated by lyophilization in a freeze drier (SIMENS FD5-3). Thus, block copolymers of PDMA-*b*-PNIPAM and PtBA-*b*-PNIPAM were obtained from macro-CTA of PDMA and PtBA, respectively. The compositions and molecular weights were determined by ^{1}H NMR and GPC.

Table 1
Comparison of kinetic parameters of cryopolymerizations of DMA and *t*BA in dioxane.

Monomer	Apparent rate constant (k_{app}, s^{-1})	Induction duration (T_{ind}, h)
DMA	6.33×10^{-5}	1.13
*t*BA	2.56×10^{-5}	2.27

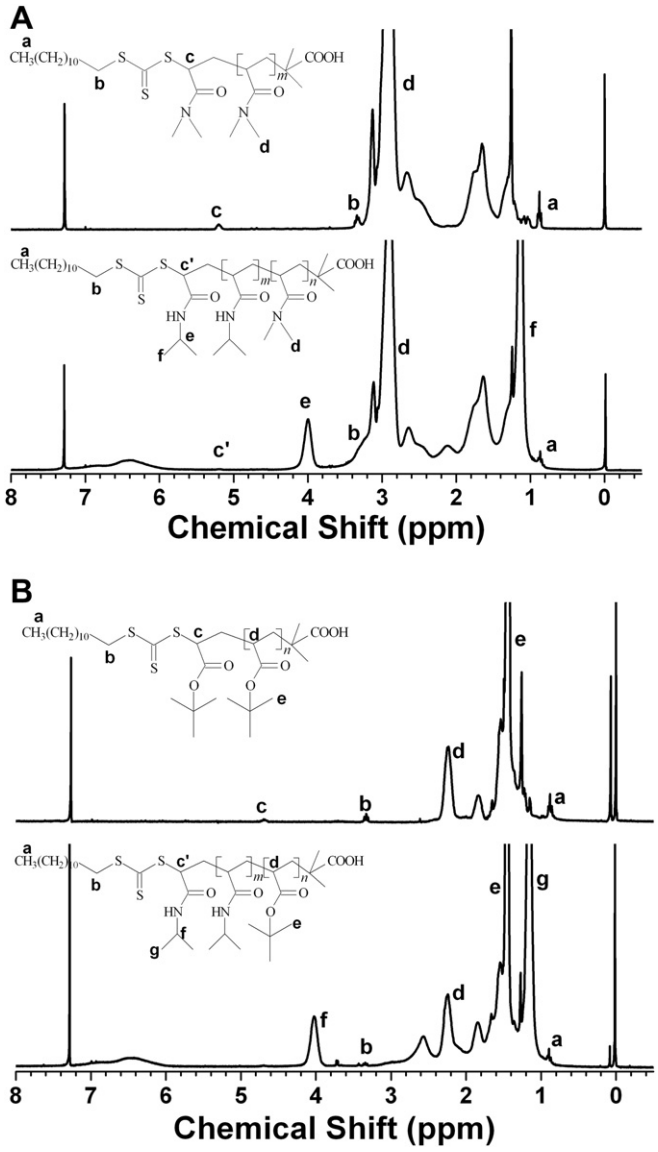

Fig. 2. Typical ^{1}H NMR spectra of PDMA and the corresponding PDMA-*b*-PNIPAM, PtBA and the corresponding PtBA-*b*-PNIPAM.

2.4. Characterizations

^{1}H NMR (300 MHz) measurements were performed on Bruker DMX300 spectrometer in $CDCl_3$ using tetramethylsilane as internal reference. The molecular weight and molecular weight distribution were determined by GPC using a series of three Styragel GPC columns (set at 30 °C). Waters 1515 pump and Waters 2414 differential refractive index detector were used. The eluent was (DMF + 1 g/L LiBr) for PDMA polymers or THF for PtBA polymers at a flow rate of 1.0 mL/min.

3. Results and discussion

RAFT cryopolymerization, different from bulk, solution and emulsion RAFT polymerizations, is carried out in unfrozen liquid microphase of the macrofrozen system as shown in Scheme 1.

Immediately after the oxidant of initiation couple was introduced, the polymerization mixture was immersed in the cryoreactor, resulting in crystallization of most of the solvent at subzero

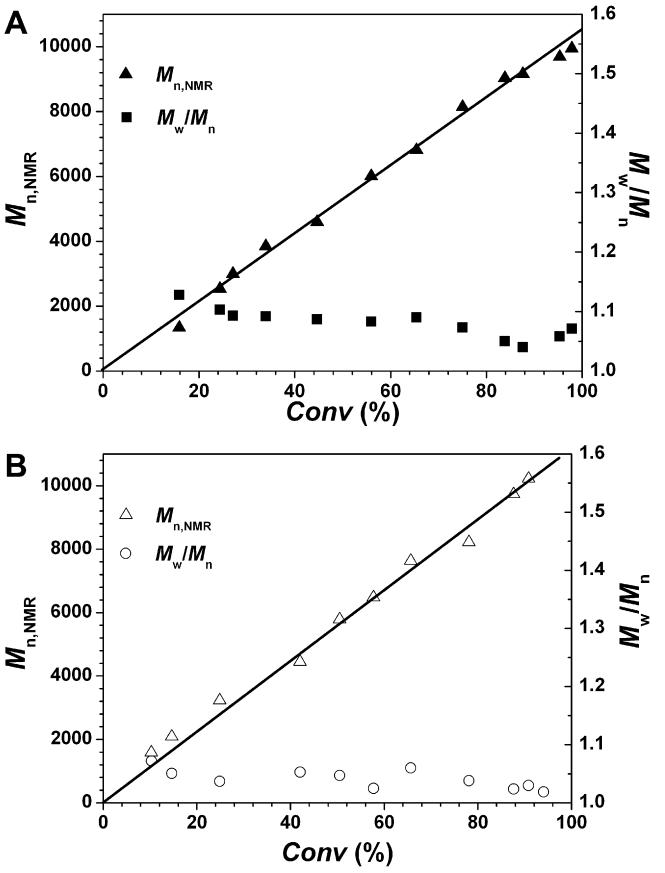

Fig. 3. Number-averaged molecular weight and polydispersity index of polymer as a function of monomer conversion for DMP mediated cryopolymerizations of DMA (▲, ●) and tBA (△, ○) at −5 °C.

temperature. Although the polymerization mixture appeared as a frozen system, there still existed small unfrozen domains, which were called as liquid microphases, encircled by solvent crystals. Monomers and other dissolved substances might be concentrated in these unfrozen microphases and the polymerization proceeded there. Depending on the cryopolymerization conditions, 0.1–10% of the total polymerization mixture remained unfrozen [2,10]. As the volume of the unfrozen liquid microphase was much less than that of the solid phase, the local monomer concentration was much higher than the monomer concentration in the initial reaction mixture. Thus, cryo-concentration effect could offset the decrease of polymerization rate caused by low temperature [6,8]. Herein, we applied RAFT cryopolymerizations of acrylamide and acrylate monomers in frozen dioxane at −5 °C and their controlled/living features have been confirmed based on polymerization kinetics, molecular weight of polymers and sequential block polymerizations.

3.1. Kinetic study of RAFT cryopolymerizations of DMA and tBA

Fig. 1 shows the linear dependence of $\ln([M]_0/[M])$ (where $[M]_0$ and [M] is the initial monomer concentration and the monomer concentration at the certain time, respectively) on the polymerization time for both cryopolymerizations of DMA and *t*BA. The results indicate that the cryopolymerizations are of first-order kinetics with respect to monomer concentration and the number of active radicals remains constant during the polymerization even at the high conversion (~95%). From the kinetic

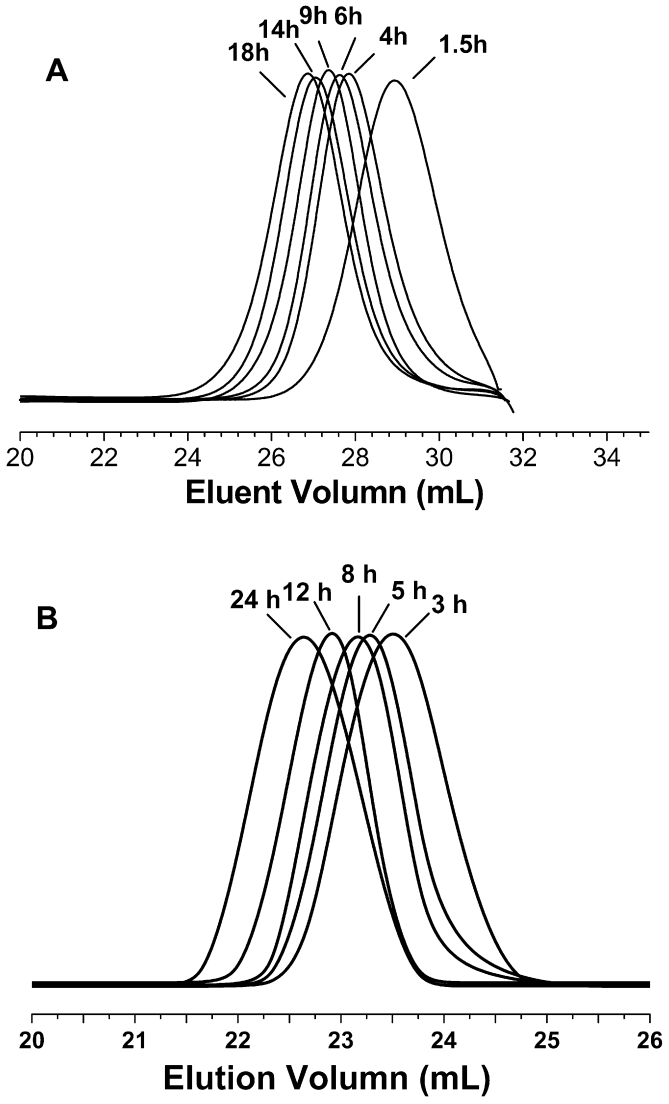

Fig. 4. GPC traces of PDMA (A) and PtBA (B) synthesized via RAFT cryopolymerization using CHPO/ASA as the redox initiators and DMP as the CTA at different polymerization times.

plots, we obtain the apparent rate constants (k_{app}) and induction durations (T_{ind}) of the polymerizations by linear fitting experimental data and the results are listed in Table 1. It clearly demonstrates that k_{app} of DMA is obviously higher than that of *t*BA, while the former induction duration is rather shorter than the latter one. The longer induction period in the cryopolymerizations of DMA and *t*BA is presumably due to both the lower rate of initiator decomposition and the slower fragmentation of the intermediate RAFT radical in the pre-equilibrium at the low temperature [26].

3.2. Molecular weight and its distribution

The chemical structure of PDMA and PtBA was characterized by ^{1}H NMR (Fig. 2). As for PDMA, the signals of methyl protons in DMA unit are observed at 2.0–3.2 ppm, and the methine group of DMA unit attached to trithiocarbonate group, is visible at 5.2 ppm. From their integrals, the number-averaged molecular weights ($M_{n,NMR}$) of PDMA at different sampling are calculated and the data are illustrated in Fig. 3.

As for PtBA shown in Fig. 2B, the peak at 2.1–2.4 ppm is ascribed to the methine protons of the tBA units. The signals at 3.4 and 0.9 ppm indicate the existence of the trithiocarbonate and the methyl group from CTA in the polymer chain. The methine group of tBA unit, attached to trithiocarbonate group, is also visible at 4.7 ppm. Similarly, $M_{n,NMR}$ of PtBA was calculated from the integrals of the signal at 4.7 ppm and that at 2.1–2.4 ppm. The data are also illustrated in Fig. 3.

Fig. 3 shows the dependences of number-average molecular weight by ^{1}H NMR spectroscopy ($M_{n,NMR}$) and polydispersity index (M_w/M_n) by GPC measurement on monomer conversion (*Conv*) of RAFT cryopolymerizations. It could be found that $M_{n,NMR}$ of the both polymers increases linearly with *Conv* and M_w/M_n remains narrow throughout the polymerization.

Shown in Fig. 4 are GPC evolutions of PDMA and PtBA at different intervals of RAFT cryopolymerizations. The observed increase in molecular weight is identified by the peak shift toward lower elution volume. Significantly, GPC traces are unimodal and free from both the low molecular weight tailing and the high molecular weight termination products, which is consistent with a controlled polymerization process.

All the results demonstrate explicitly the well-controlled features of RAFT cryopolymerizations of DMA and tBA with DMP as the CTA and CHPO/ASA as the redox initiators at −5 °C in dioxane.

We also investigated the RAFT cryopolymerization of other monomers such as NIPAM, nBA and MA. The results are listed in Table 2. It was noticed that the theoretical molecular weight ($M_{n,th}$) are close to the values of $M_{n,NMR}$ and the molecular weight distributions are very narrow at the high conversion. All the evidences indicate the well-controlled behavior of those RAFT cryopolymerizations.

3.3. Sequential block copolymerizations with NIPAM

It has been widely accepted that the ultimate test of living nature is the ability to quantitatively chain extend homopolymers to yield block copolymers. In order to perform sequential block polymerization, the cryopolymerizations of NIPAM with the macro-CTAs obtained above were processed and the results are listed in Entry 7 and 9 of Table 2.

The chemical structure of PDMA-*b*-PNIPAM was characterized by ^{1}H NMR (Fig. 2A). Besides the presence of the signals of PDMA, that of methyl protons in NIPAM unit appears at 4.0 ppm. Thus, $M_{n,NMR}$ of PDMA-*b*-PNIPAM was calculated based on the integrals of

Table 2
RAFT cryopolymerization of different monomers in dioxane at −5 °C.

Entry	Monomer	Time/h	*Conv*/%[a]	$M_{n,th}$[b]	$M_{n,NMR}$[c]	$M_{n,GPC}$[d]	M_w/M_n[d]
1	DMA	18	97.8	10,200	10,300	28,800	1.07
2	NIPAM	18	63.4	6400	5200	4600	1.04
3	tBA	32	94.0	9800	11,100	10,900	1.05
4	nBA	36	98.5	10,300	12,400	8900	1.03
5	MA	36	97.8	11,000	12,500	10,300	1.07
6	DMA	6	65.4	6800	7100	21,500	1.09
7[e]	NIPAM	24	21.7	13,800	12,700	29,300	1.14
8	tBA	6	28.4	2900	3100	3800	1.04
9[f]	NIPAM	24	33.7	6100	5800	6600	1.09

[a] Determined gravimetrically.
[b] Calculated according to $M_{n,th} = (Conv \times W_{monomer}/M_{CTA}) + M_{m,CTA}$, where $W_{monomer}$ is the weight of monomer, M_{CTA} is moles of the CTA and $M_{m,CTA}$ is the molecular weight of CTA.
[c] Determined by ^{1}H NMR.
[d] Determined by GPC.
[e] Block copolymerization in the presence of the macro-RAFT agent of PDMA (Entry 6).
[f] Block copolymerization in the presence of the macro-RAFT agent of PtBA (Entry 8).

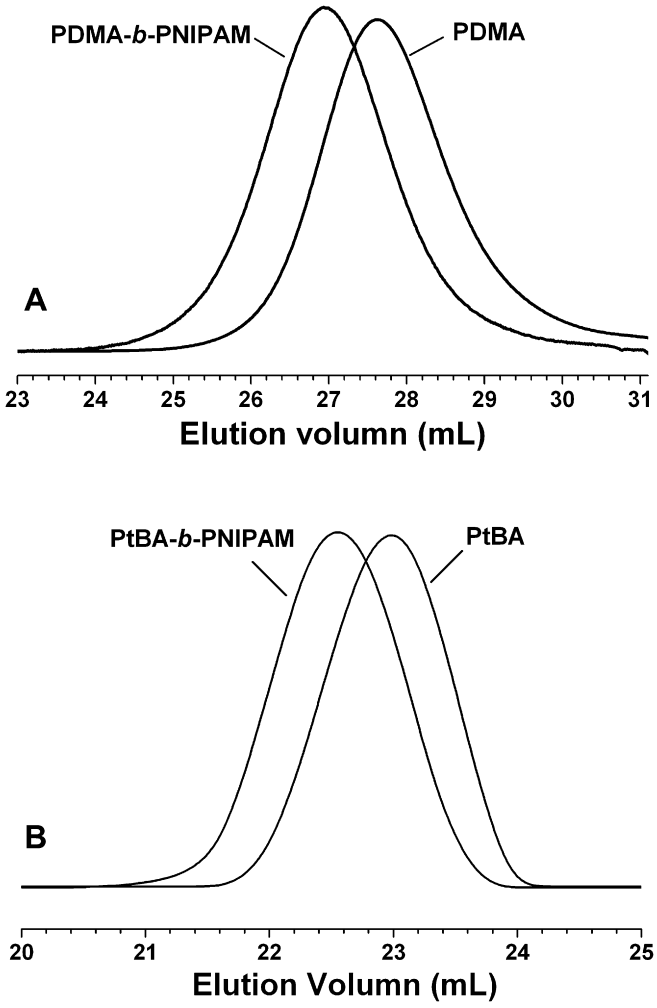

Fig. 5. GPC traces for block copolymers of PDMA-*b*-PNIPAM, PtBA-*b*-PNIPAM and the corresponding PDMA and PtBA macro-CTAs.

signals at 4.0 ppm and 5.2 ppm, with the addition of $M_{n,NMR}$ of PDMA. Fig. 2B shows the typical ^{1}H NMR spectra of PtBA and PtBA-*b*-PNIPAM. Similarly, $M_{n,NMR}$ of PtBA or PtBA-*b*-PNIPAM was calculated and the results are listed in Table 2.

From the data of entry 7 and 9 in Table 2, the values of $M_{n,th}$ of PDAM-*b*-PNIPAM and PtBA-*b*-PNIPAM are fairly close to those of their $M_{n,NMR}$, indicating the high initiation efficiency of macro-CTA (entry 6 and 8). GPC traces of these two block copolymers are shown in Fig. 5. GPC traces of two block copolymers are symmetrical and no tailing at both sides was obviously observed. Additionally, M_w/M_n of block copolymers still keeps very low. The results suggest the near-quantitative blocking efficiency of macro-CTAs and the well-controlled characteristics of RAFT cryopolymerization.

4. Conclusions

RAFT cryopolymerizations of acrylamides and acrylates were successfully carried out at −5 °C with CHPO/ASA as redox initiation couple, and DMP as CTA. The linear dependence of $\ln([M]_0/[M])$ on reaction time and that of $M_{n,NMR}$ on monomer conversion have been observed. Based on GPC and NMR characterizations, molecular weight increases with monomer conversion and its distribution keeps narrow throughout the cryopolymerization. The sequential block copolymerizations of NIPAM with the obtained macro-CTAs have also been successfully performed to result in the corresponding block copolymers with controlled molecular weight and narrow molecular weight distribution. All these evidences show that RAFT cryopolymerizations of DMA and tBA in dioxane possess well-controlled characteristics.

Acknowledgments

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