Kinetic Investigation of Poly(2-(Dimethylamino)Ethyl Acrylate) (PDMAEA) Synthesized by RAFT Polymerization

Wenze Xiao[#], Shoujing Sun[#], Junhong Liu, Yihan Li, Jingjiang Sun, Qingfu Wang[*] and Wei Zhao[*]

Key Laboratory of Rubber-plastics, Ministry of Education, School of Polymer Science and Engineering, Qingdao University of Science and Technology, Zhengzhou Rd. 53, CN-266042 Qingdao, China

Abstract: Poly(2-(dimethylamino)ethyl acrylate) (PDMAEA) is an important pH-responsive and cationic polymer with broad applications in biomedicine and materials engineering, yet its controlled synthesis remains challenging. In this study, reversible addition–fragmentation chain transfer (RAFT) polymerization was employed to systematically investigate the polymerization kinetics of DMAEA under various conditions. A major obstacle identified was the degradation of the monomer into acrylic acid and dimethylaminoethanol, which significantly slows polymerization kinetics. While molecular weight increased linearly with monomer conversion up to moderate levels, achieving low dispersity at high conversion proved difficult, with values typically ranging between 1.3 and 1.8. Improved control over the polymerization, evidenced by a successful chain-extension experiment, was achieved by reducing the target degree of polymerization, lowering the reaction temperature, and employing macro-chain transfer agents.

Keywords: PDMAEA, RAFT polymerization, Kinetics, Molecular weight distribution.

INTRODUCTION

2-(Dimethylamino)ethyl acrylate (DMAEA) is an important amphiphilic monomer with tertiary amine. Its polymer, poly(2-(dimethylamino)ethyl acrylate) (PDMAEA), and copolymer have been widely used in pharmaceuticals,[1, 2] surfactants [3] and water treatment industries [4] due to their pH-responsive and cationic properties, as their tertiary amine groups can be quaternized at low pH, or in the presence of halogen-alkyl compounds such as methyl chloride or dimethyl sulfate [5-7]. Especially, PDMAEA cationic polymer was also found to be able to degrade in aqueous solution, [8] which has attracted significant attention in the potential application for gene delivery [9-14] by carrying DNA or oligonucleotides to the cells and releasing the encapsulated payload after degradation [15-17].

Poly(2-(dimethylamino)ethyl acrylate) (PDMAEA) has traditionally been synthesized via conventional free-radical polymerization. However, this approach offers limited control over molecular weight and dispersity, and is unsuitable for preparing architecturally defined polymers such as block copolymers [18], and hence, few reports have been published. Previous studies employed atom transfer radical polymerization (ATRP) to control the active radical polymerization of DMAEA [19, 20]. However, the authors observed that accumulation of chains terminated by quaternization of the amino pendant group during polymerization resulted in increased polydispersity of PDMAEA. By using nitroxide-mediated polymerization, Bian and Cunningham avoided the use of a catalyst, and they demonstrated that good control over DMAEA polymerization could be achieved [21, 22]. However, we have noticed the fact that its self-catalyzed effects could affect the properties of DMAEA, and possibly its methacrylate homologue. Hence, in order to address the aforementioned issues and simultaneously achieve the precise synthesis and structural regulation of PDMAEA, this study adopts reversible addition-fragmentation chain transfer (RAFT) polymerization technology to construct the DMAEA polymerization system. To obtain polymer products with well-defined structures (controllable molecular weight and narrow dispersity), we systematically investigated the effects of several key polymerization parameters, including the initial ratio of initiator to chain transfer agent (CTA) ([initiator]/[CTA]), the initial ratio of monomer to CTA ([monomer]/[CTA]), the regulation of reaction temperature, and the selection of CTAs with different structures (such as (propanoic acid)yl butyl trithiocarbonate (PABTC), methyl 2-(butylthiocarbonothioylthio)propanoate (MCEBTTC) and 2-cyanoprop-2-yl dithiobenzoate (CPDB). These investigations focused on the impacts of the above parameters on polymerization kinetics, polymer molecular weight, and molecular weight distribution, aiming to provide an optimized scheme for the controlled synthesis of PDMAEA and further expand its application boundaries in fields such as biomedicine and materials engineering.

*Address Correspondence to this Author at the Key Laboratory of Rubber-plastics, Ministry of Education, School of Polymer Science and Engineering, Qingdao University of Science and Technology, Zhengzhou Rd. 53, CN-266042 Qingdao, China;
E-mail: wangqf@qust.edu.cn; zwqust@qust.edu.cn

[#]These authors contributed equally to this work.

Received on 10-12-2025 Accepted on 16-01-2026 Published on 19-01-2026

E-ISSN: 000-000/26

EXPERIMENTAL SECTION

Materials

Unless otherwise stated, all reagents were used as received. 2-(Dimethylamino)ethyl acrylate (DMAEA, Aldrich, 98%) was purified by vacuum distillation. Methyl acrylate (MA, Sigma-Aldrich, 99%) was filtered through a basic aluminium oxide (activated, basic, Brockmann I, standard grade, ~150 mesh, 58A) column before use, to remove the radical inhibitor. Azobisisobutyronitrile (AIBN) was recrystallised twice from methanol prior to use. Chain transfer agents (CTA) (propanoic acid)yl butyl trithiocarbonate (PABTC) was received from Dulux, Australia: methyl 2-(butylthiocarbonothioylthio)propanoate (MCEBTTC), 2-cyanoprop-2-yl dithiobenzoate (CPDB) were synthesized as reported [45, 46]. 2-methoxy poly(ethylene glycol) 2-propanoate butyltrithiocarbonate ($mPEG_{16}$-PBTC) was supplied by Dulux, Australia and was characterised via electrospray ionization mass spectrometry (ESI-MS) ($[M_n + Na]^+$ = 979 g mol^{-1}: DP_n = 16), *via* ^1H NMR (M_n = 900 g mol^{-1}; DP_n = 15) and *via* Size Exclusion Chromatography (SEC) (M_n = 1100 g mol^{-1}; $Đ$ = 1.10). Poly(dimethylsiloxane), monohydroxy terminated (PDMS, M_n = 4670 g mol^{-1}), *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDCI, ≥ 98%) and 4-dimethyl aminopyidine (DMAP) were purchased from Sigma-Aldrich and used as received. Toluene (99%), methanol (99%), chloroform (99%), and tetrahydrofuran (THF, 99%) were purchased from Sigma-Aldrich and used as received unless specified otherwise. All reactions were carried out under N_2 atmosphere unless otherwise stated.

Methods

In this thesis, most of the NMR spectra were recorded using a Bruker 200 MHz, 300 MHz, and 400 MHz spectrometers at 25 °C. Samples were dissolved in deuterated solvents including deuterated chloroform (CDCl3), deuterium oxide (D2O), deuterated dimethyl sulfoxide (DMSO-d6), and deuterated acetone (acetone-d6). All chemical shifts are reported in ppm (δ).

Size exclusion chromatography (SEC) SEC analysis was performed on a Shimadzu LC-20AD liquid chromatography system. The eluent (THF), containing 0.5 vol% toluene as a flow marker, was pre-filtered through a 0.2 µm pore-size filter. The measurements were carried out at 40 °C using an Elder CH-150 heater. Prior to injection (100 µL), the sample was filtered through a 0.2 µm polytetrafluoroethylene (PTFE) membrane. The system was calibrated with narrow polystyrene (PS) standards (Đ < 1.1). The molar mass ($M_{n,SEC}$) and dispersity (Đ) of the synthesized polymers were determined by conventional calibration using ASTRA for Windows software (Version 6.90.08) with known calibration constants for the RI detector.

Electrospray Ionization Mass Spectrometry (ESI-MS) was done on a Finnigan LCQ MS Detector with Finnigan LCQ Data Processing using Instrument Control Software. 20 µL of solution (100 µg of sample dissolved in 1 mL of HPLC grade methanol) was fed into the electrospray ionization unit at 0.06 mL min^{-1}. The electrospray voltage was 4.5 kV, the sheat flow rate was set to 50, and the temperature of the heated capillary was 300°C.

Synthesis of PDMS Containing Macro-CTA (PDMS-PBTC)

Poly(dimethylsiloxane) macro-chain transfer agent (PDMS macro-CTA) was synthesized via an EDCI/DMAP-catalyzed esterification reaction between the carboxylic acid-terminated PDMS and the carboxylic acid group of the PABTC RAFT agent. In a typical procedure, a solution of N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI, 0.288 g, 1.50 mmol) in dichloromethane (5 mL) was added dropwise over 15 minutes to a stirred solution of PDMS (5.0 g, 1.07 mmol), PABTC (0.381 g, 1.60 mmol), and 4-dimethylaminopyridine (DMAP, 0.019 g, 0.16 mmol) in dichloromethane (10 mL), maintained at -20°C using a cooling bath. Following the addition, the reaction mixture was allowed to warm to room temperature and stirred for 20 hours. The crude mixture was then subjected to a workup procedure, which involved sequential washing twice with 1M sodium hydroxide aqueous solution and twice with distilled water. The organic layer was separated, dried over anhydrous magnesium sulphate, and filtered. The solvent was removed under reduced pressure to yield the crude product. Final purification was achieved by flash chromatography on silica gel, using dichloromethane as the eluent, to remove any unreacted PABTC RAFT agent. The isolated product fraction was concentrated under vacuum to afford the desired PDMS macro-CTA as a yellow oil. (yield = 67 %). ^1H NMR (300 MHz, $CDCl_3$,) 4.25 (2H, t, O-CH_2-$\underline{CH_2}$-CO_2), 3.69 (2H, t, O-$\underline{CH_2}$-CH_2-CO_2), 4.84 (1H, q, S-$\underline{CH}(CH_3)$-CO_2), 3.42 (2H, t, O-$\underline{CH_2}$-$(CH_2)_2$-Si), 3.35(2H, t, CH_2-$\underline{CH_2}$-S), 0.93 (3H, t,$\underline{CH_3}$-$(CH_2)_3$-S), 1.43(2H, m, CH_3-CH_2-$\underline{CH_2}$-CH_2-S), 1.60-1.67(2H, m, CH_3-$\underline{(CH_2)_3}$-Si, S-CH($\underline{CH_3}$)-CO2), 0.07(3H, m, Si$\underline{(CH_3)_2}$-O).

Typical Procedure for the RAFT Polymerization of DMAEA in Toluene at 65 °C with $[DMAEA]_0/[CTA]_0/[AIBN]_0$ = 100/1/0.2

Polymerization was conducted using N,N-dimethylaminoethyl acrylate (DMAEA) as the monomer, with azobisisobutyronitrile (AIBN) as the initiator and PABTC as the chain transfer agent. In a typical procedure, DMAEA (5.727 g, 40.0 mmol), AIBN (0.013 g, 0.080 mmol), and PABTC (0.095 g, 0.40 mmol) were precisely weighed and dissolved in toluene (1.75 g) in a Schlenk tube equipped with a magnetic stir bar. The resulting solution was thoroughly degassed via five consecutive freeze-pump-thaw cycles to remove dissolved oxygen. Following degassing, the Schlenk tube was backfilled with inert nitrogen gas and immediately sealed. The polymerization was initiated by immersing the sealed tube into a pre-heated thermostat oil bath maintained at 65°C under constant stirring. To monitor the reaction kinetics, periodic samples were withdrawn from the reaction mixture at predetermined time intervals using a degassed syringe under a positive nitrogen flow to maintain an anaerobic environment. Monomer conversion was determined by ^{1}H NMR spectroscopy by comparison of the ratio of vinyl peaks centered at δ 5.81 (1H, dd) to the alkyl peak at δ 4.26 (2H, t) and its polymeric counterpart at δ 4.18 (2H, br), as shown in Eq.1.

$$\text{Monomer conversion} = (I_{4.18}+I_{4.26}-2\ I_{5.81})/\ (I_{4.18}+I_{4.26}) \times 100\% \quad \text{Eq. 1}$$

Where the $I_{5.81}$, $I_{4.26}$ and $I_{4.18}$ are, respectively, the integrals of monomer vinyl peaks centered at δ 5.81 (1H, dd), alkyl peak at δ 4.26 (2H, t) and its polymeric counterpart at δ 4.18 (2H, br).

By neglecting the number of chains initiated by AIBN and considering a fully consumption of CTA, the theoretical average molar mass in number, $M_{n,theo}$ can be determined using Eq.2 below,

$$M_{n,theo.} = \times M_{DMAEA} \times \text{Conversion} + M_{CTA,} \quad \text{Eq. 2}$$

Where $[DMAEA]_0$ and M_{DMAEA} are, respectively, the initial molar concentration and molar mass of DMAEA monomer; $[CTA]_0$ and M_{CTA} are, respectively, the initial molar concentration and molar mass of CTA.

Typical Procedure of Block Extension of PDMAEA Homopolymer used as Macro-CTA with MA

Block extension of $PDMAEA_{17}$ ($M_{n,theo}$ = 2630 g mol^{-1}) with MA (Entry 1, Table **2**).

The chain extension polymerization of methyl acrylate (MA) using a PDMAEA macro-chain transfer agent (macro-CTA) was performed. In a typical procedure, methyl acrylate (MA, 0.8 g, 9.293 mmol), the PDMAEA macro-CTA (0.122 g, 0.046 mmol), azobisisobutyronitrile (AIBN, 0.636 mg, 3.872×10^{-3} mmol), and toluene (0.533 g) were combined in a vial sealed with a rubber septum. The reaction mixture was thoroughly degassed by sparging with dry nitrogen gas for 20 minutes while maintained at 0°C in an ice bath. Subsequently, the vial was transferred to a preheated thermostat oil bath at 65°C to initiate the polymerization. After a reaction time of 4 hours, the polymerization was terminated by rapid cooling of the vial in an ice bath. The monomer conversion was determined by ^{1}H NMR spectroscopy, specifically by comparing the integrated signals of the vinyl protons in the monomer (δ 6.41, 6.12, and 5.81 ppm, each 1H, dd) to the signal of the three methoxy protons, which are present in both the monomer and the polymer (observed at 3.75 ppm and 3.66 ppm, respectively). The molar mass and dispersity (Đ) of the resulting block copolymer were analyzed by size exclusion chromatography (SEC) using THF as the eluent. Under these conditions, after 4 hours, an 84% monomer conversion was achieved, yielding a polymer with a theoretical number-average molar mass ($M_{n,\ theo}$) of 17,100 g·mol^{-1}, an SEC-measured M_n of 14,500 g·mol^{-1}, and a dispersity (Đ) of 1.25.

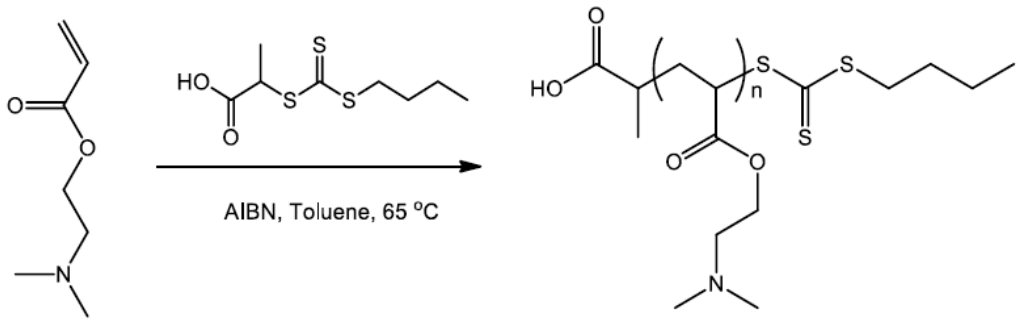
RESULTS AND DISCUSSION

Typical conditions for polymerizing DMAEA by RAFT are shown in Scheme 1. As the study of the bulk homopolymerization of DMAEA was limited due to ~~the~~ high viscosity encountered (over 60% conversion), [23] working at dilute conditions were preferred. In this study, toluene was chosen as solvent due to low chain transfer constant and being a good solvent for PDMAEA. First of all, standard conditions usually employed in acrylates RAFT homopolymerization were applied to DMAEA monomer (Entry 1, Table **1**). The polymerization was performed at 65 °C with a ratio $[DMAEA]_0/[PABTC]_0/[AIBN]_0$ = 100/1/0.2. Figure **1a** shows a fast polymerization for the first 90 min. with 68% conversion attained. After that time, the rate starts to decrease to finally reached 85% after 5h. The pseudo-first order plot (Figure **1b**) is highly informative and clearly indicates a constant decrease in rate of polymerization within the whole process. We can note that this decrease become more pronounced after 60 min. of polymerization. This feature proves that the concentration of active species did not remain constant during the DMAEA RAFT polymerization and could be associated to the loss of radical species by chain transfer [24]. This hypothesis looks like confirmed by the analysis of the evolution of M_n and dispersity ($Đ$)

values with conversion (Figure **1c**). Indeed, a linear increase of the M_n is observed until 60% (around 60 min. polymerization) after what the M_n start to stagnate until 85%. Evolution of PDMAEA chromatograms with conversion in SEC-THF (Figure **2**) also show a monomodal distribution with an increasing tail to the side of low molar mass polymer chains. In the same time, the dispersity values, which were stable at around 1.4, start to increase continuously until 1.8. These experimental observations, that become more pronounced with the depletion of monomer in the medium, strongly suggest the loss of radical species by degradative chain transfer. Moreover, the fact that the evolution of M_w values did not show a positive deviation (characteristic to some branching event) strongly suggests that the major event occurring is chain transfer event followed by β-scission [25]. The entire β-chain scission process occurs because the tertiary amines act as a strong nucleophile—meaning they tend to attack positively charged or partially positively charged centres. Due to the electron-withdrawing nature of the substituents, the carbon in the thiocarbonyl group carries a partial positive charge. During this process, unreacted tertiary amines attack the CTA, leading to the decomposition of the RAFT reagent and disruption of its core controlling structure. The eliminated Z• radicals may initiate new uncontrolled chain growth, resulting in broader molecular weight distribution and loss of polymerization controllability. However, all these experimental observations cannot totally explain this apparent loss of control with *Đ* values as high as 1.8 and it is also important to mention that the analytical technique (SEC-THF) used for characterizing polymer chains could add to this phenomenon. Indeed, an interesting comparison between two different chromatographic systems used for characterizing PDMAEA polymer chains clearly show that this parameter has to be taking account. For instance, the same PDMAEA sample (Entry 5, Table **1**, $M_{n,theo}$ = 6320 g mol^{-1}) was analysed by SEC-THF and SEC-DMAc (Figure **3**). Comparison of both analysis show that in DMAc, a close experimental value for M_n is obtained ($M_{n,SEC\text{-}DMAc}$ = 6100 g mol^{-1}) with a much lower dispersity value ($Đ_{SEC\text{-}DMAc}$ = 1.24*)* in comparison with what was obtained in THF ($M_{n,SEC\text{-}THF}$ = 3650 g mol^{-1}; $Đ_{SEC\text{-}THF}$ = 1.42). The solvent polarity of DMAc is thought to be much stronger than THF, which can provide better dissolvability for PDMAEA and reduce the interactions between PDMAEA and PS column, therefore, resulted in more accurate M_n and *Đ* [26]. In the RAFT polymerization of ethyl 2-(dimethylamino)acrylate using a macromolecular chain transfer agent (macro-CTA), β-scission plays a particularly significant role. During the chain transfer step, the initially formed adduct radical is highly unstable due to steric and electronic effects imparted by the tertiary amine functionality adjacent to the radical center. This instability promotes immediate β-scission, which cleaves the bond β to the radical site, generating a new terminal active radical capable of reinitiating polymerization and leaving behind an unsaturated end group (typically a vinyl moiety) on the “dead” polymer chain derived from the macro-CTA. Critically, this pathway consumes only one active propagating radical but produces two dead chains—one from the original macro-CTA fragment and one terminated growing chain—thereby reducing the concentration of active centers in the system. As a result, the overall polymerization rate declines, and the final polymer fails to achieve the theoretically predicted molecular weight.

It is particularly worth to mention that DMAEA is a kind of active monomer. During the period of kinetic study, we observed that DMAEA monomer (distilled and stored in the fridge) slowly degrade into acrylic acid and 2-(dimethylamino) ethanol after 2~3 weeks as confirmed by ESI-MS (Figure **4**) and by the yellow colour developed [4, 11, 27, 28]. This degradation plays a direct impact on the DMAEA RAFT polymerization (Figure **1a**) and slow down the rate of polymerization compared to the freshly distilled one with only 45 % conversion reached after 250 min (85% with the freshly distilled DMAEA). However, in terms of molar mass control (Figure **1c**), the same level of control is observed (linear evolution of the experimental Mn with the conversion and Đ value around 1.4). This observation strongly suggests that one of the products of degradation of DMAEA act as a radical scavenger. The process described here occurs precisely because the small-molecule byproducts generated from the degradation of DMAEA after two weeks of storage combine with the radicals produced by the RAFT agent. This combination causes the radicals to lose activity, forming what is referred to above as "dead" chains. Consequently, the number of radicals decreases, the concentration of effective chain transfer agents is reduced, control over the polymerization deteriorates, and the molecular weight distribution broadens. It is worth to mention that the same result was observed when a freshly new bottle of DMAEA was used and only passed through basic alumina in order to remove the inhibitor (the yellow colour due to any impurity is also removed) [29, 30].

To identify optimized conditions for the preparation of well-defined PDMAEA by the RAFT process [31], several parameters were investigated (Table **1**): the effect of the ratio of initiator to CTA and monomer to



Scheme 1: General condition for RAFT polymerization of DMAEA.

Table 1: Conditions for the Polymerization of DMAEA via RAFT with AIBN as Initiator and the Resulting Monomer Conversion, Molecular Mass and Distribution Data

Entry	CTA	$[DMAEA]_0$: $[CTA]_0$; $[AIBN]_0$	Solvent	T (°C)	Time (min)	Conv. (%)NMR	$M_{n\ theo.}$ (g mol^{-1})	$M_{n\ SEC.}$ (g mol^{-1})	*Đ*
1	PABTC	100:1:0.2 [a]	Toluene	65	90	25	3570	2370	1.51
					250	44	6540	350	1.43
2	PABTC	100:1:0.2 [b]	Toluene	65	90	69	10430	7000	1.49
					250	86	12480	6130	1.79
3	PABTC	100:1:0.1 [b]	Toluene	65	90	40	5970	3370	1.44
					250	69	10120	5180	1.52
4	PABTC	100:1:0.05 [b]	Toluene	65	90	30	4530	2570	1.48
					250	40	5970	3430	1.45
5	PABTC	50:1:0.1 [b]	Toluene	65	90	60	4530	2620	1.38
					250	84	6320	3650	1.42
6	PABTC	20:1:0.04 [b]	Toluene	65	90	48	1610	1120	1.42
					250	74	2350	1590	1.44
7	PABTC	100:1:1.45 [b]	Toluene	50	90	63	9260	5230	1.40
					250	84	12270	6800	1.49
8	MCEBTTC	100:1:0.2 [b]	Toluene	65	90	56	8260	4780	1.36
9	MCEBTTC	100:1:0.2 [b]	Toluene & Acetic acid	65	90	62	9120	5140	1.40
10	PDMS-PBTC	100:1:0.2 [b]	Toluene	65	90	49	11900	9920	1.34
11	PEG-PBTC	100:1:0.2 [b]	Toluene	65	90	54	8750	5600	1.28
12	CPDB	100:1:0.2 [b]	Toluene	65	8h	32	4800	4100	1.20
					24	58	8500	5800	1.57

[a] DMAEA (2 weeks after distillation), [b] DMAEA (freshly distilled).

CTA; the influence of the temperature and the type of CTA used.

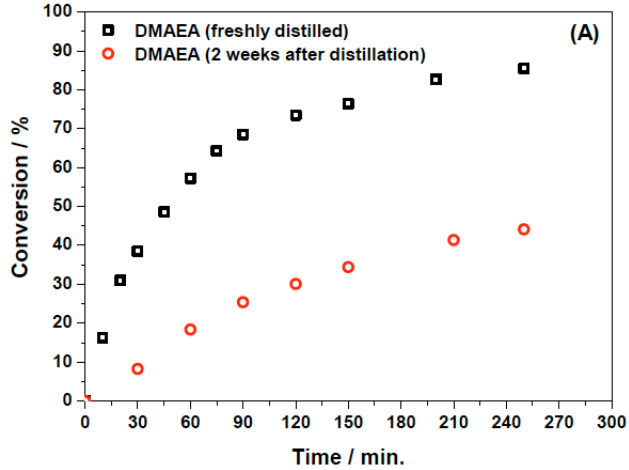
Influence of [M]/[CTA] Ratio

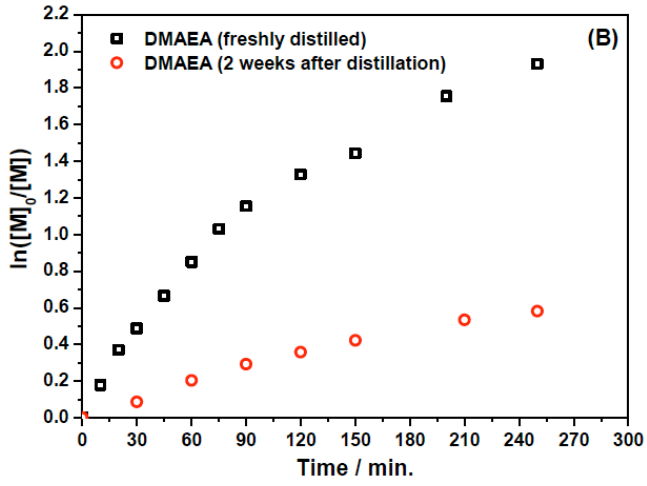
The influence of the relative concentrations of monomer to chain transfer agent was evaluated by varying the $[DMAEA]_0/[PABTC]_0$ values from 100, 50, to 20 in toluene with a constant monomer concentration, 4.94 M, at 65 °C. To choose an initiator concentration, and for the sake of reliable comparison, the [DMAEA]/[AIBN] ratio was kept constant (Entry 2, 5 and 6, Table **1**). As expected, as shown in Figure **5**, similar kinetics for [M]/[CTA] ratio of 100, 50 and 20, conversion 86%, 84% and 74% respectively after 250 mins, was observed because of the exactly same conditions, the same concentration of monomer and initiator, which were utilized during the polymerization. In terms of the control, as decreasing the targeted DP, the $M_{n\ exp.}$ analyzed by SEC-THF was close to the $M_{n\ theo.}$ line and *Đ* values were also decreased from 1.79 to 1.42 for the final polymers as shown in Figure **5**. The improved "better control" is thought to be due to two

Table 2: Chain Extension with MA using PDMAEA as Macro CTA via RAFT Polymerizations

Entry	Macro CTA	$[MA]_0$:$[PDMAEA]_0$:$[AIBN]_0$	Conv. (%)	$M_{n\ theo.}$ (g mol-1)	$M_{n\ SEC.}$ (g mol-1)	$Đ$
1	$PDMAEA_{17}$	200:1:0.08	84	17100	14500	1.25
2	$PDMAEA_{43}$	500:1:0.2	88	45500	43800	1.55
3	$PDMAEA_{85}$	500:1:0.2	80	46800	44500	1.64

possible reasons. One is attributed to the increased CTA concentration. In our case, on one hand, the concentration of initiator was kept constant, which means the same number of dead chains were created during the polymerization. On the other hand, the increased CTA concentration led to produce more living chains with CTA species, which reduced the fraction of the dead chains, therefore improved the control [30, 31]. Moreover, the more CTA in polymerization medium also resulted in the less frequency for the domain chains adding radicals, therefore reduced the chance of termination and improved the control of polymerization. The other possible reason for the "better control" is due to the problem of SEC, which might be caused by the intensity of affinity between different chain length of polymers and PS columns by using THF as eluent [33].





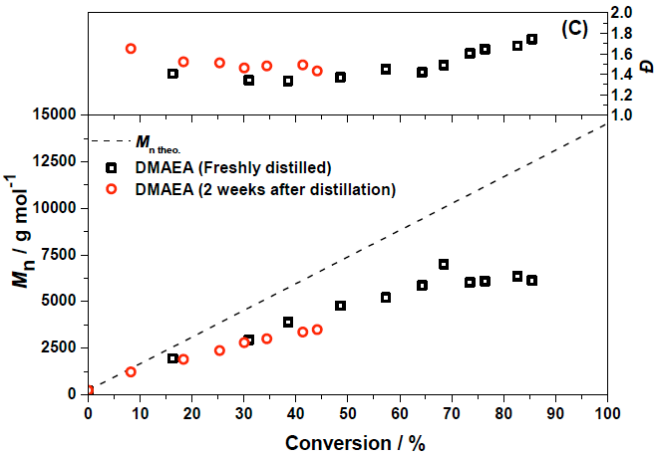


Figure 1: Influence of monomer degradation on the RAFT polymerization of monomer DMAEA with PABTC as CTA: (**A**) plots of conversion vs. polymerization time, (**B**) kinetic plots and (**C**) plots of *M*n and *Đ* vs. conversion.

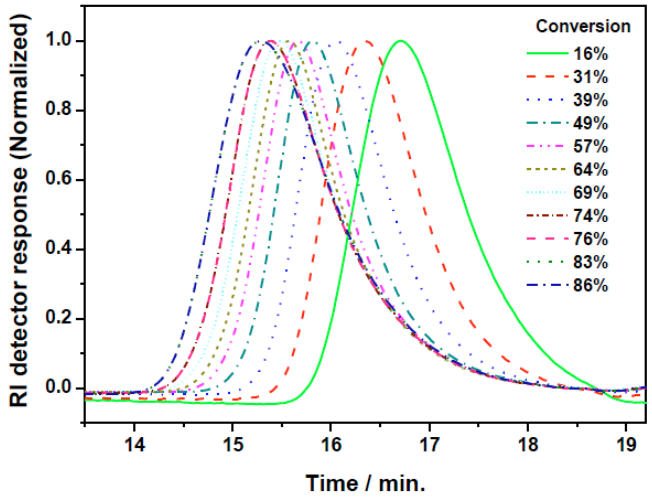


Figure 2: SEC chromatograms of pDMAEA at different conversions.

In order to further investigate the control of polymerization, chain extension reactions have been done with monomer MA using the above pDMAEA (DP=100, 50 and 20) as the macro-CTA at 65°C in toluene. As shown in Figure **6**, a complete shift of SEC trace for pDMAEA with DP=20 was observed. Molecular weight of the starting pDMAEA ($M_{n\ exp.}$ = 1 600 g/mol, $Đ$ = 1.44) has shifted toward higher molecular weight ($M_{n\ exp.}$ = 14 500 g/mol, $Đ$ = 1.25), which proves the 'living' character. However, for the other two pDMAEA with DP = 50 and 100, double peaks in SEC traces were obtained after the chain

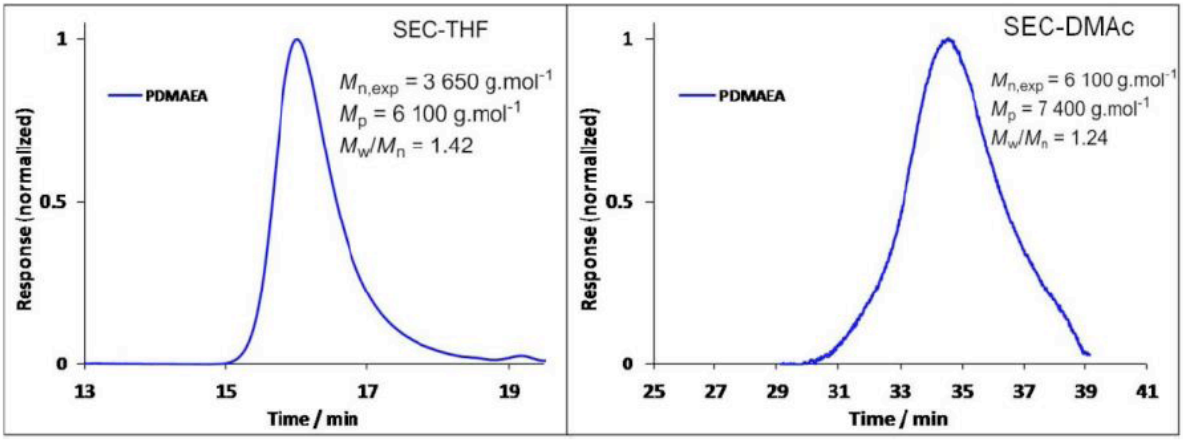


Figure 3: Comparison of SEC results of PDMAEA (DPn ≈ 42, Entry 5, Table 1) with different eluent.

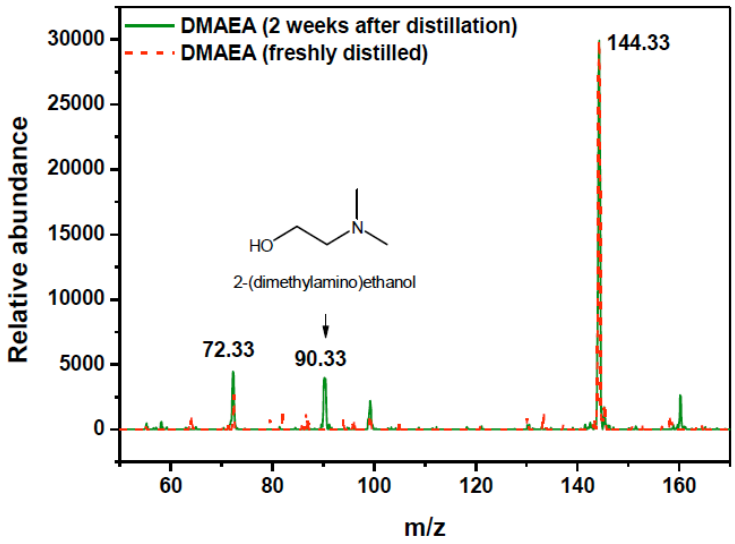


Figure 4: EI mass spectra for freshly distilled DMAEA (straight line) and the one after 2 weeks' distillation (dash line).

extension, which demonstrates the presence of dead chains from the first block. In addition, when DP of pDMAEA was increased from 50 to 100, more proportion of dead chains were observed in SEC traces, which confirms that the control of polymerization was lost as the targeted DP was increased for the RAFT process of pDMAEA.

Influence of [CTA] / [AIBN] Ratio

The amount of AIBN with respect to CTA, PABTC, was varied from 0.2 to 0.1 and 0.05 Molar percent (entry 2, 3 and 4, Table **1**), with all other parameters held constant. The polymerizations were carried out in toluene with monomer concentration of 4.94 M at 65 °C with [DMAEA] / [PABTC] = 100. A decrease in the amount of AIBN resulted in the decrease on the rate of polymerization. As shown in Table **1**, after the same reaction time, 250 min, the obtained conversions of monomer were 86%, 69% and 40%, respectively, which were consistent with the fact that polymerization rate R_p is proportional to the initiator concentration of power of ½, $R_p \propto [AIBN]^{1/2}$ [34]. In the other hand, according to the RAFT polymerization mechanism [35], the decrease of initiator concentration should much more disfavour termination reactions than reactions involving only one radical species (propagation, addition-fragmentation). Consequently, it is expected to improve the control [36]. However, the $M_{n,exp.}$ of final polymers (after 250 min) obtained by THF-SEC were still far away from the $M_{n,theo.}$ and the values of *Đ* remained high, *Đ* ≈ 1.5, as decreased the concentration of AIBN. According to the results of $M_{n,exp.}$ and *Đ*, it looks like decreasing the concentration of initiator did not really improve the control of DMAEA polymerization. However, it is difficult to draw definitive conclusions regarding this parameter because the polymer chain lengths differ, which, as mentioned earlier, could influence the $M_{n,exp}$ and *Đ* values obtained by SEC analysis [37].

Influence of the Temperature

The other investigated parameter was decreasing the temperature with the aim of reducing the degradation of monomer or any other side reactions

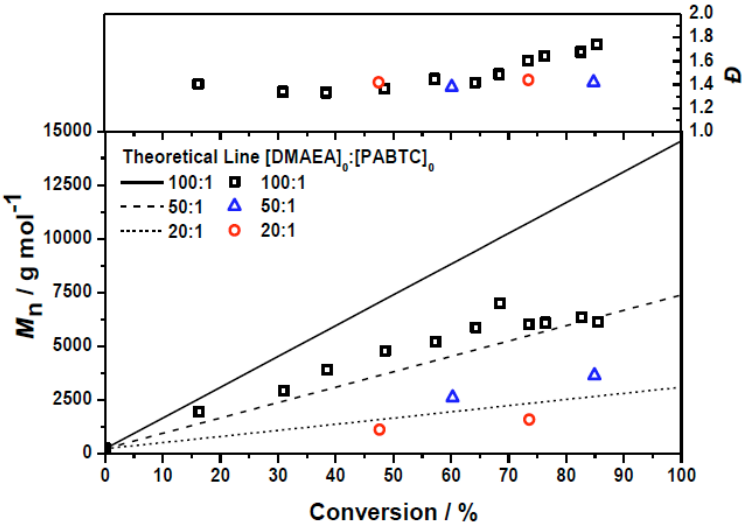


Figure 5: Influence of [M]/[CTA] on the polymerization of pDMAEA via RAFT: plots of M_n and $Đ$ versus monomer conversion.

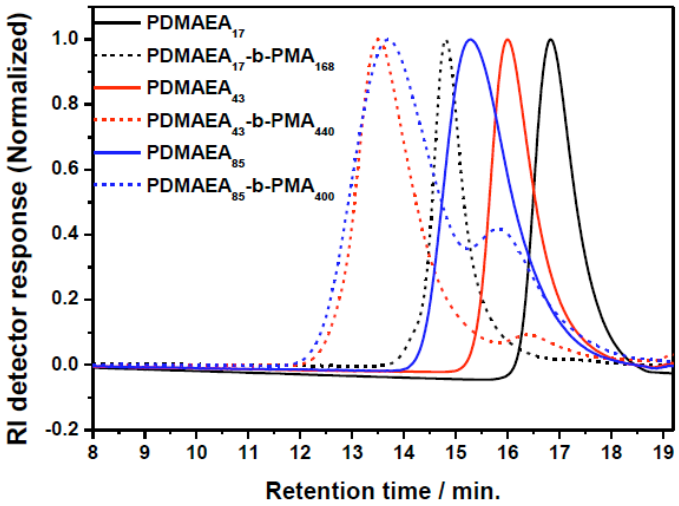


Figure 6: SEC chromatograms of final polymers obtained with different targeted DP values for polymerizations of pDMAEA via RAFT with PABTC as RAFT agent in toluene and their chain extension with MA.

during the polymerization (Entry2 and 7, Table **1**) [38]. At the generally employed temperature, 65°C, DMAEA polymerization in the presence of toluene reached 85% conversion in 250 min. At 50°C, the same conversion was obtained in more than 20 h. This strong decrease in the polymerization rate originates from both the lower primary radical concentration at initial stages and the decrease of all the rate constants. So, to choose the conditions for being able to compare the results with being performed at 65°C, influence of temperature on both the initiator decomposition rate constant and the other rate constants must be considered.

First, the lower AIBN decomposition rate constant at 50 °C induces the initiation of fewer radicals. In fact, at the beginning of the polymerization, the concentration of primary radicals at 50 °C is significantly lower than that at 65 °C (k_d (50°C) = 2.67×10^{-6} s^{-1}, corresponding to a half-life time of 72 h, k_d (65°C) = 1.93×10^{-5} s^{-1}corresponding to a half-life time of 10 h). Therefore, in order to keep the similar concentration of generated primary radicals or defined as the 'dead chains' during the same period of polymerization, relatively high concentration of AIBN should be used at 50 °C and the value can be calculated by the following equation:

$$\int_0^t 2[AIBN]_1\ (1 - e^{-k_{d\,1}\,t}) = \int_0^t 2[AIBN]_2\ (1 - e^{-k_{d\,2}\,t}),$$

which can be rearranged into:

$$\frac{[AIBN]_1}{[AIBN]_2} = \frac{k_{d\,2}}{k_{d\,1}}$$

Where $[AIBN]_1$, $k_{d\,1}$ are initial concentration and decomposition rate of AIBN at 65°C, and $[AIBN]_2$, $k_{d\,2}$ are initial concentration and decomposition rate of AIBN at 50°C. As expected, very close kinetics were achieved after 250 min with conversion 85%. Moreover, concerning the control of molecular weight distribution, decreased temperature should lead to better controlled polymerization, which is also confirmed by the value of

Đ that was decreased from 1.79 at 65 °C to 1.49 at 50 °C. This is due to the fact that lower temperature reduces the degradation of monomer and radical reactivity, which improves the selectivity of the various radical reactions and lead to a better control [39].

Influence of the types of CTA

The polymerization study of pDMAEA was extended to other RAFT agents including MCEBTTC [40], CPDB [41], and macro CTAsuch [42] as $mPEG_{16}$-PBTC and PDMS-PBTC (Figure **7**). In order to improve the property of control by either changing the functionality in the R group or varying the fragmentation rate coefficient value of CTA, five more experiments (entry8, 9, 10, 11and 12, Table **1**) were performed with the same conditions as using PABTC and the performances were compared in terms of both kinetics and molecular weight distributions. As shown in Table **1**, the carboxylic function group (–COOH) beared in CTA R group or in polymerization medium (entry 9, MCEBTTC with equivalent amount of acetic acid) increased the kinetics slightly compare to the other RAFT agents (entry 2 & 9 vs. 8, 10, 11; conversion: 69 & 62% vs. 56, 49, 54%). It is possibly due to the esterification reaction between carboxylic group and dimethylamino ethanol compound which comes from the degradation of DMAEA monomer during the polymerization [8, 31, 43], therefore avoids the retardant on the kinetics caused by the compound of dimethylamino ethanol as we mentioned above. In respect of molecular weight distribution, the –COOH group in CTA or in polymerization medium also affects the control, which makes the distribution become broad with increased *Đ* values. The specific differences can be seen in Table 1 and Figure **8**. However, in the case

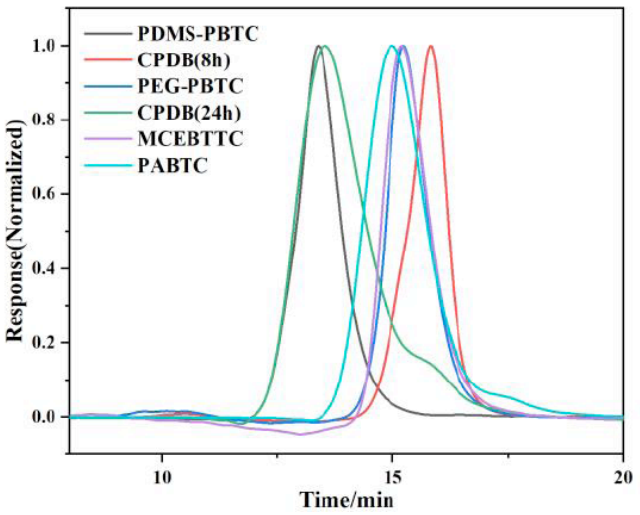


Figure 8: GPC spectra of pDMAEA obtained at the same polymerization conditions (65°C, toluene, **$[DMAEA]_0$: $[CTA]_0$; $[AIBN]_0$ =** 100:1:0.2) with different chain transfer agents.

of the macro-RAFT agent, $mPEG_{16}$-PBTC and PDMS-PBTC (entry 10 and 11), it is worth mentioning that the narrow dispersity may also result from differences in the dn/dc values of the diblock copolymer which is very different from pDMAEA in eluent THF at room temperature [44]. Moreover, dithiobenzoate RAFT agent [44], CPDB, was also used instead of trithiocarbonate. The intermediate radical with CPDB species is believed to be more stable than that of trithiocarbonate, and a lower fragmentation rate coefficient is expected to lead to a better controlled polymerization [45]. Unfortunately, after 24 h, when the conversion reached to 58% which is similar as other RAFT agents, well controlled polymerization was not obtained with still high *Đ* = 1.57 value. According to this result, we suppose that the chain transfer termination

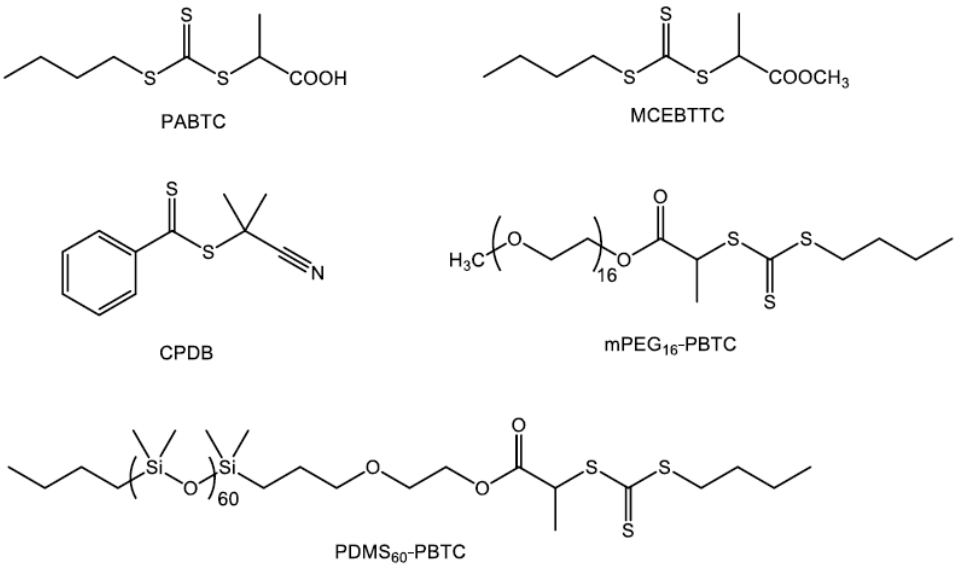


Figure 7: Structure of chain transfer agents: (Propionic acid)yl butyl trithiocarbonate (PABTC), 2-(butylthiocarbonothioylthio) propanoate (MCEBTTC), 2-cyanoprop-2-yl dithiobenzoate (CPDB), 2-methoxy poly(ethylene glycol) 2-propanoate butyltrithiocarbonate (PEG_{16}-PBTC), and poly(dimethylsiloxane) 2-propanoate butyltrithiocarbonate ($PDMS_{60}$-PBTC).

and some other side reaction termination could happen during the polymerization which causes the loss of control and broad distributions. So, more investigations need to be done to work out the better control of pDMAEA by RAFT polymerization [46, 47].

CONCLUSION

In summary, the controlled RAFT polymerization of DMAEA remains challenging due to monomer instability and side reactions. DMAEA degrades to acrylic acid and dimethylaminoethanol, which retard kinetics and limit control, yielding polymers with dispersity (Đ) of 1.3-1.8. Using freshly distilled monomer, lowering the temperature (65 °C → 50 °C), and reducing the target DP ([M]/[CTA] = 100 → 20) improve control, enabling successful chain extension with MA. Carboxylic CTAs and macro-CTAs offer modest improvements, though SEC analysis in THF may overstate gains. Kinetic deviations above ~50% conversion and lower-than-theoretical Mn indicate dominant degradative chain transfer and β-scission. Therefore, conventional RAFT polymerization of DMAEA, even under meticulously optimized conditions, fails to deliver homopolymers with very narrow molecular weight distributions (Đ < 1.2). Achieving true control will necessitate strategies that transcend routine parameter tuning. Promising avenues for future investigation include: (i) the strategic deployment of well-defined macro-CTAs to synthesize block copolymers that intrinsically suppress side reactions through microenvironmental or steric effects; (ii) the rational design of next-generation CTAs engineered to resist aminolysis and other nucleophilic side reactions with tertiary amines; and (iii) the adoption of alternative reaction media (*e.g.*, polar protic solvents) or advanced polymerization modalities-such as photo-RAFT or ARGET RAFT-to minimize steady-state radical concentrations and thereby suppress degradative chain-transfer pathways.

ACKNOWLEDGMENT

This work was supported by the International Science and Technology Assistance Program of the Ministry of Science and Technology (No. KY202001016); Shandong Provincial Natural Science Foundation Magnitude Fundamental Research, China (No. ZR2022ZD11); Doctoral Fund of Qingdao University of Science and Technology (12030430010828); the Shandong Provincial Natural Science Foundation (ZR2020QB026); the Shandong Natural Science Excellent Youth Fund (ZR2019YQ22); and the Introduction and Cultivation Plan of Young Innovative Talents in Colleges and Universities of Shandong Province (2019).

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCE

[1] Skandalis A, Selianitis D, Pispas S. PnBA-b-PNIPAM-b-PDMAEA thermo-responsive triblock terpolymers and their quaternized analogs as gene and drug delivery vectors. Polymers, 2021, 13(14): 2361. https://doi.org/10.3390/polym13142361

[2] Ghasemi S, Soltanimehr H, Rastegari B, *et al*. Multi-responsive nanocarrier based on P (NIPAM-co-DMAEA) grafted magnetic cellulose for controlled and targeted drug release. International Journal of Biological Macromolecules, 2025: 147417. https://doi.org/10.1016/j.ijbiomac.2025.147417

[3] Li X, Zhang C, Peng H, *et al*. Design and synthesis of fluorosurfactants for microfluidic droplet-based bioapplications. Polymer Science & Technology, 2025, polymscitech. 5c00092. https://doi.org/10.1021/polymscitech.5c00092

[4] Ros S, Kleinberger R M, Burke N A D, *et al*. Charge-shifting polycations with tunable rates of hydrolysis: effect of backbone substituents on poly [2-(dimethylamino) ethyl acrylates]. Macromolecules, 2018, 51(15): 5752-5761. https://doi.org/10.1021/acs.macromol.8b00931

[5] Brannigan R P, Khutoryanskiy V V. Synthesis and evaluation of mucoadhesive acryloyl-quaternized PDMAEMA nanogels for ocular drug delivery. Colloids and Surfaces B: Biointerfaces, 2017, 155: 538-543. https://doi.org/10.1016/j.colsurfb.2017.04.050

[6] Giaouzi D, Pispas S. PNIPAM-b-PDMAEA double stimuli responsive copolymers: Effects of composition, end groups and chemical modification on solution self-assembly. European Polymer Journal, 2020, 135: 109867. https://doi.org/10.1016/j.eurpolymj.2020.109867

[7] Liu D, Wen G, Skandalis A, *et al*. Influences of subphase salt conditions on the interfacial behavior of triblock copolymer PnBA-PNIPAM-PDMAEA. Langmuir, 2025, 41, 24, 15347-15353. https://doi.org/10.1021/acs.langmuir.5c00922

[8] Ros S, Wang J, Burke N A D, *et al*. A Mechanistic study of the hydrolysis of Poly [N, N-(dimethylamino) ethyl acrylates] as charge-shifting polycations. Macromolecules, 2020, 53(9): 3514-3523. https://doi.org/10.1021/acs.macromol.9b02272

[9] Werfel T A, Swain C, Nelson C E, *et al*. Hydrolytic charge-reversal of PEGylated polyplexes enhances intracellular un-packaging and activity of siRNA. Journal of Biomedical Materials Research Part A, 2016, 104(4): 917-927. https://doi.org/10.1002/jbm.a.35629

[10] Traeger A, Leiske M N. The whole is greater than the sum of its parts–challenges and perspectives in polyelectrolytes. Biomacromolecules, 2024, 26(1): 5-32. https://doi.org/10.1021/acs.biomac.4c01061

[11] Gurnani P, Blakney A K, Terracciano R, *et al*. The *in vitro*, ex vivo, and *in vivo* effect of polymer hydrophobicity on charge-reversible vectors for self-amplifying RNA. Biomacromolecules, 2020, 21(8): 3242-3253. https://doi.org/10.1021/acs.biomac.0c00698

[12] Neugebauer D. Grafted polymethacrylate nanocarriers in drug delivery. Nanomaterials for Clinical Applications. Elsevier, 2020: 271-295. https://doi.org/10.1016/B978-0-12-816705-2.00009-6

[13] Vardaxi A, Pispas S. Random cationic copolymers as nanocarriers for ovalbumin. Journal of Drug Delivery Science and Technology, 2023, 80: 104177. https://doi.org/10.1016/j.jddst.2023.104177

[14] Ros S, Freitag J S, Smith D M, *et al*. Charge-shifting polycations based on N, N-(dimethylamino) ethyl acrylate for improving cytocompatibility during DNA delivery. ACS omega,

2020, 5(16): 9114-9122.
https://doi.org/10.1021/acsomega.9b03734

[15] Liao X, Walden G, Falcon N D, *et al*. A direct comparison of linear and star-shaped poly (dimethylaminoethyl acrylate) polymers for polyplexation with DNA and cytotoxicity in cultured cell lines. European Polymer Journal, 2017, 87: 458-467.
https://doi.org/10.1016/j.eurpolymj.2016.08.021

[16] Mapfumo P P, Reichel L S, André T, *et al*. Optimizing biocompatibility and gene delivery with DMAEA and DMAEAm: a niacin-derived copolymer approach. Biomacromolecules, 2024, 25(8): 4749-4761.
https://doi.org/10.1021/acs.biomac.4c00007

[17] Le Bohec M, Kenzo K B, Piogé S, *et al*. Structure-pDNA complexation and structure–cytotoxicity relationships of PEGylated, cationic aminoethyl-based polyacrylates with tunable topologies. Polymer Chemistry, 2019, 10(15): 1968-1977.
https://doi.org/10.1039/C8PY01776J

[18] Chroni A, Pispas S. Hydrophilic/hydrophobic modifications of a PnBA-b-PDMAEA copolymer and complexation behaviour with short DNA. European Polymer Journal, 2020, 129: 109636.
https://doi.org/10.1016/j.eurpolymj.2020.109636

[19] Matyjaszewski K. Atom transfer radical polymerization (ATRP): current status and future perspectives. Macromolecules, 2012, 45(10): 4015-4039.
https://doi.org/10.1021/ma3001719

[20] Lorandi F, Fantin M, Matyjaszewski K. Atom transfer radical polymerization: a mechanistic perspective. Journal of the American Chemical Society, 2022, 144(34): 15413-15430.
https://doi.org/10.1021/jacs.2c05364

[21] Ajogbeje, Opeyemi J., and Robin A. Hutchinson. "An investigation of solvolytic reactions and exploration of 2-(dimethylamino) ethyl methacrylate/methyl acrylate free radical copolymerization kinetics." *European Polymer Journal* (2025): 114253.
https://doi.org/10.1016/j.eurpolymj.2025.114253

[22] Lamontagne H R, Lessard B H. Nitroxide-mediated polymerization: a versatile tool for the engineering of next generation materials. ACS Applied Polymer Materials, 2020, 2(12): 5327-5344.
https://doi.org/10.1021/acsapm.0c00888

[23] Sun Y, Lin B, Wang Q, *et al*. Preparation of poly (2-aminoethyl methacrylate-co-2-(diethylamino) ethyl methacrylate) by atom transfer radical polymerization for gene delivery. Acta Polymerica Sinica, 2015 (1): 113-119.

[24] Perrier S. 50th anniversary perspective: RAFT Polymerization-A user guide. Macromolecules, 2017, 50(19): 7433-7447.
https://doi.org/10.1021/acs.macromol.7b00767

[25] Vancoillie G, Vergaelen M, Hoogenboom R. Ultra-high performance size-exclusion chromatography in polar solvents[J]. Journal of Chromatography A, 2016, 1478: 43-49.
https://doi.org/10.1016/j.chroma.2016.11.034

[26] Sun F, Feng C, Liu H, *et al*. PHEA-g-PDMAEA well-defined graft copolymers: SET-LRP synthesis, self-catalyzed hydrolysis, and quaternization. Polymer Chemistry, 2016, 7(45): 6973-6979.
https://doi.org/10.1039/C6PY01637E

[27] Ros S, Burke N A D, Stöver H D H. Synthesis and properties of charge-shifting polycations: Poly [3-aminopropylmethacrylamide-co-2-(dimethylamino) ethyl acrylate]. Macromolecules, 2015, 48(24): 8958-8970.
https://doi.org/10.1021/acs.macromol.5b02191

[28] Whitfield R, Anastasaki A, Truong N P, *et al*. Efficient binding, protection, and self-release of dsRNA in soil by linear and star cationic polymers. ACS Macro Letters, 2018, 7(8): 909-915.
https://doi.org/10.1021/acsmacrolett.8b00420

[29] Cook A B, Peltier R, Hartlieb M, *et al*. Cationic and hydrolysable branched polymers by RAFT for complexation and controlled release of dsRNA. Polymer Chemistry, 2018, 9(29): 4025-4035.
https://doi.org/10.1039/C8PY00804C

[30] Shevtsov V Y, Hsin T Y, Shieh Y T. Preparation of amphiphilic copolymers via base-catalyzed hydrolysis of quaternized poly [2-(dimethylamino) ethyl methacrylate]. Polymer Chemistry, 2022, 13(10): 1429-1436.
https://doi.org/10.1039/D1PY01697K

[31] Hub L, Koll J, Radjabian M, *et al*. Blue light-induced iniferter RAFT polymerization in aqueous-alcoholic media as a universal tool for the homopolymerization of various monomer families: kinetic investigations on different scales. Polymer Chemistry, 2023, 14(26): 3063-3074.
https://doi.org/10.1039/D3PY00241A

[32] Han S, Wu J, Zhang Y, *et al*. Utilization of poor RAFT control in heterogeneous RAFT polymerization. Macromolecules, 2021, 54(10): 4669-4681.
https://doi.org/10.1021/acs.macromol.1c00381

[33] Obata M, Ishihara E, Hirohara S. Effect of tertiary amino groups in the hydrophobic segment of an amphiphilic block copolymer on zinc phthalocyanine encapsulation and photodynamic activity. RSC advances, 2022, 12(28): 18144-18153.
https://doi.org/10.1039/D2RA02224A

[34] Peng W, Cai Y, Fanslau L, *et al*. Nanoengineering with RAFT polymers: from nanocomposite design to applications. Polymer Chemistry, 2021, 12(43): 6198-6229.
https://doi.org/10.1039/D1PY01172C

[35] Tian X, Ding J, Zhang B, *et al*. Recent advances in RAFT polymerization: novel initiation mechanisms and optoelectronic applications. Polymers, 2018, 10(3): 318.
https://doi.org/10.3390/polym10030318

[36] Jacky P E, Neukirch M A, Fors B P. Anionic reversible addition–fragmentation chain-transfer polymerization of methacrylates. Journal of the American Chemical Society, 2025, 147(33): 29648-29652.
https://doi.org/10.1021/jacs.5c10586

[37] Burgevin F, Hapeshi A, Song J I, *et al*. Cationic star copolymers obtained by the arm first approach for gene transfection. Polymer Chemistry, 2023, 14(32): 3707-3717.
https://doi.org/10.1039/D3PY00352C

[38] Rabyk M, Destephen A, Lapp A, *et al*. Interplay of thermosensitivity and pH sensitivity of amphiphilic block–gradient copolymers of dimethylaminoethyl acrylate and styrene. Macromolecules, 2018, 51(14): 5219-5233.
https://doi.org/10.1021/acs.macromol.8b00621

[39] Yamawake K, Hayashi M. The role of tertiary amines as internal catalysts for disulfide exchange in covalent adaptable networks. Polymer Chemistry, 2023, 14(6): 680-686.
https://doi.org/10.1039/D2PY01406H

[40] Tran N T D, Jia Z, Monteiro M J. Programmable disassembly of polymer nanoparticles through surfactant interactions. Industrial & Engineering Chemistry Research, 2019, 58(46): 21003-21013.
https://doi.org/10.1021/acs.iecr.9b01991

[41] Xia Y, Xu X, Yu H, *et al*. Preparation of zwitterionic microspheres of PDMAEMA-b-PMAA by RAFT dispersion polymerization in alcohol, their pH-sensitivity in water, and self-assembly in KCl solution. Colloid and Polymer Science, 2021, 299(4): 663-674.
https://doi.org/10.1007/s00396-020-04790-6

[42] Sivkova R, Konefal R, Kostka L, *et al*. Precise control of molecular weight characteristics of charge-shifting poly (2-(N, N-dimethylamino) dthylacrylate) synthesized by reversible addition-fragmentation chain transfer polymerization. Macromolecular Rapid Communications, 2025, 46(2): 2400640.
https://doi.org/10.1002/marc.202400640

[43] Hochół A, Flejszar M, Chmielarz P. Advances and opportunities in synthesis of flame retardant polymers via reversible deactivation radical polymerization. Polymer Degradation and Stability, 2023, 214: 110414.
https://doi.org/10.1016/j.polymdegradstab.2023.110414

[44] Liu J, Li J, Wang C Y, *et al*. RAFT surfactant-free cationic emulsion polymerization of styrene: Effect of hydrophobicity of block macro-RAFT agent. Journal of Macromolecular Science, Part A, 2020, 58(4): 232-242. https://doi.org/10.1080/10601325.2020.1840923

[45] Lee Y, Boyer C, Kwon M S. Photocontrolled RAFT polymerization: past, present, and future. Chemical Society Reviews, 2023, 52(9): 3035-3097. https://doi.org/10.1039/D1CS00069A

[46] Guzik A, Raffa P. Direct synthesis via RAFT of amphiphilic diblock polyelectrolytes facilitated by the use of a polymerizable ionic liquid as a monomer. Polymer Chemistry, 2021, 12(38): 5505-5517. https://doi.org/10.1039/D1PY00801C

[47] Kerr A, Moriceau G, Przybyla M A, *et al*. Bis (trithiocarbonate) disulfides: from chain transfer agent precursors to iniferter control agents in RAFT polymerization. Macromolecules, 2021, 54(14): 6649-6661. https://doi.org/10.1021/acs.macromol.1c00565