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Synthesis of thermoresponsive block and graft copolymers via the combination of living cationic polymerization and RAFT polymerization using a vinyl ether-type RAFT agent

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ABSTRACT

A novel vinyl ether-type RAFT agent, benzyl 2-(vinylloxy)ethyl carbonotrithioate (BVCT) was synthesized for various block copolymers via the combination of living cationic polymerization of vinyl ethers and reversible addition–fragmentation chain transfer (RAFT) polymerization. The novel BVCT-trifluoroacetic acid adduct play an important role to produce well-defined block copolymers, which is both a cationogen under EtAlCl_2 initiation system in the presence of ethyl acetate for living cationic polymerization and a RAFT agent for blocks by RAFT polymerization. The resulting polymer, poly(vinyl ether)s, by living cationic polymerization had a high number average α -end functionality (≥ 0.9) as determined by both ^1H NMR and MALDI-TOF-MS spectrometry. In addition, this poly(vinyl ether)s worked well as a macromolecular chain transfer agent for RAFT polymerization. The RAFT polymerization of radically polymerizable monomers was conducted in toluene using 2,2'-azobis(isobutyronitrile) at 70 °C. For example, a double thermoresponsive block copolymer ($\text{MOVE}_{61}\text{-}b\text{-NIPAM}_{150}$) consisting of 2-methoxyethyl vinyl ether (MOVE) and *N*-isopropylacrylamide (NIPAM) was prepared via the combination of living cationic polymerization and RAFT polymerization. The block copolymer reversibly formed and deformed micellar assemblies above the phase separation temperature (T_{ps}) of poly(NIPAM) block in water. This BVCT is not only functioned as an initiator, but also acted as a monomer. When BVCT was copolymerized with MOVE by living cationic polymerization, followed by graft copolymerization with NIPAM via RAFT polymerization, well-defined graft copolymers ($\text{MOVE}_n\text{-}co\text{-BVCT}_m\text{-}g\text{-NIPAM}_x$ ($n = 62\text{-}73$, $m = 1\text{-}9$, $x = 19\text{-}214$)) were successfully obtained. However, no micelle formed in water above T_{ps} of poly(NIPAM) graft chain unlike the case of block copolymers.

Keywords:

living cationic polymerization / reversible addition fragmentation chain transfer (RAFT) / block copolymer

1. Introduction

Block copolymers are macromolecules consisting of different blocks, which is generally prepared effectively by precision polymerization after the discovery by Michael Szwarc 50 years ago [1,2]. Block copolymers can be synthesized by adding the second monomer sequentially into the first living polymer [3]. The control of chain length and the sequence for each of the blocks during synthesis gives a different function for the polymer such as stimuli-responsive micelles and gels [4]. However, these techniques have only a limited monomer that capable to synthesize through the same propagating species. Recent development of precision polymerization allow us to combine multiple polymerization fashions and to prepare various block copolymers [5,6]. For example, vinyl ethers are difficult to synthesize in radical polymerization while acrylics and acrylamides cannot be cationically polymerized. Thus, an effective and successful transformation from cationic to radical or another way around should be approached to synthesize block copolymers.

The mechanistic transformation involving living and controlled polymerization has attracted many researchers' interest. Examples include synthesis of block copolymers of polystyrene (PSt) and either poly(methyl acrylate) or poly(methyl methacrylate) using living cationic polymerization and atom transfer radical polymerization (ATRP) first [7]. Synthesis of other polymer architectures including graft copolymers from poly(vinyl ether) macromonomer [8], polyisobutylene-based block copolymers [9] and miktoarm-star copolymers [10], hybrid block copolymers with poly(vinyl ether) blocks via organoheteroatom-mediated living radical to cationic polymerization [11,12] has been reported. In particular, transformation of living cationic to RAFT polymerization [13] and the site

transformation of polyisobutylene chain ends into RAFT polymerization [14, 15] was earlier works on the combination of the living cationic polymerization and RAFT polymerization. As indicated here, there are a variety of transformation or combination strategies, which proves to be encouraging and necessary for the design of various block copolymers.

In the recent years, we also have reported some methods to prepare well-defined block copolymers between vinyl ethers and other monomers such as acrylates, styrenes and acrylamides, and controlled molecular weight involving two mechanism polymerizations, such as living cationic polymerization and RAFT polymerization [16-19]. For the combination of living cationic polymerization and RAFT polymerization, the cationic polymerization of vinyl ether is initiated from a proton derived from the carboxylic RAFT agents and then the polymerization progressed smoothly under SnBr_4 initiation system in the presence of an additive such as ethyl acetate and 1,4-dioxane. When the polymerization is quenched after the propagation of living cationic polymerization, the RAFT group as a counteranion was concurrently recovered, followed by the RAFT polymerization of radically polymerizable monomers using 2,2'-azobis(isobutyronitrile) (AIBN) at 70 °C to prepare the block copolymers. Furthermore, using this hybrid polymerization, we also successfully synthesized ABA block copolymers using the dicarboxylic RAFT agent. In fact, these chain transfer agent (CTA) efficiencies for RAFT process are approximately 80%, which correspond almost to their end-functionalities of used macro-CTAs, poly(vinyl ether)s. However, they were sufficient to prepare the block copolymers between a cationically polymerizable monomer and a radically polymerizable monomer.

Such a macro-CTA with high end-functionality is required to synthesize well-defined block copolymers via RAFT process and to achieve a good control of their molecular weights. Although the block copolymers were successfully obtained using mono and dicarboxylic RAFT agents, they tend to decompose and irreversibly be cleaved upon treatment with a strong acid into an aldehyde

and a carboxylic acid [17]. It is because of hemiacetal ester bond, which is a relatively weak covalent bond between blocks. For example, when poly(MOVE) macro-CTA and triblock copolymer, poly(MOVE)-*b*-poly(NIPAM)-*b*-poly(MOVE), obtained from dicarboxylic RAFT agent were acidolyzed, the decomposed products obtained were corresponded to the poly(NIPAM) and poly(MOVE) homopolymer. Hence, a more strong and stable junction should be needed for the block copolymers.

In addition, as far as we are aware, researches on the synthesis of graft copolymers via transformation of living cationic into controlled radical polymerization are very limited. Lu et. al. reported a well-defined graft copolymer with poly(β -pinene) backbone chains and polystyrene and poly(meth)acrylate side chains by the transformation of living cationic polymerization to atom transfer radical polymerization (ATRP) [20,21]. They were prepared via living cationic polymerization with the 1-phenylethyl chloride/TiCl₄/Ti(OiPr)₄/*n*Bu₄N⁺Cl⁻ initiating system, and continued by using CuCl and 2,2'-bipyridine to initiate ATRP. Moreover, Hong et. al. synthesized polyisobutene-*g*-poly(methyl methacrylate) and polyisobutene-*g*-polystyrene prepared using partially brominated polyisobutylene-*b*-poly(*p*-methoxystyrene) as a macroinitiator in ATRP of the respective monomers [22]. However, so far RAFT polymerization has never been applied to this transformation.

In the present study, to prepare the stable block and novel graft polymers, we investigated the synthesis of block copolymers consisting of cationically polymerizable vinyl ethers and radically polymerizable monomers via the combination of two different polymerization mechanisms, living cationic polymerization and RAFT polymerization using a novel vinyl ether-type RAFT agent (also called BVCT) as shown in Scheme 1. The cationic polymerization of vinyl ether can be initiated from BVCT-trifluoroacetic acid adduct (BVCT-TFA), and RAFT polymerization can occur from the BVCT pendant. In particular, the resulting polymer is more stable than the previous block

copolymers because of no hemiacetal ester. In addition, since the RAFT polymerization moiety is included in initiating species for cationic polymerization, the block efficiency (i.e. number average α -end functionality) becomes higher than those of previously reported [16,17]. To demonstrate the block copolymerization, we prepared double thermoresponsive block copolymers using poly(MOVE) and poly(NIPAM) whose phase separation temperatures (T_{ps} 's) (broadly interpreted "LCSTs") in water are 66 °C [23] and 32 °C [24,25], respectively. The thermoresponsive behavior of the aqueous solutions was examined by DSC measurement and the transmittance (%) at 500 nm against temperature and was compared with the previous block copolymer with the same repeating units in aqueous solution [16].

Moreover, BVCT is a cationically polymerizable monomer. We synthesized the random copolymers of MOVE and BVCT under the same condition of the living cationic polymerization for the poly(vinyl ether) macro-CTA, followed by RAFT polymerization from BVCT unit in the random copolymer (Scheme 2). The properties of the aqueous solutions of graft copolymers were examined and compared with that of block copolymers. From these results, we proved that BVCT can be both functioned as an initiator and a monomer for cationic polymerization.

Scheme 1. Synthesis of block copolymers using BVCT-TFA via the combination of living cationic polymerization and RAFT polymerization.

Scheme 2. Synthesis of graft copolymers involving poly(MOVE) backbone and poly(NIPAM) grafts using both BVCT-TFA and BVCT, i.e. poly(MOVE-*co*-BVCT)-*g*-poly(NIPAM), via the combination of living cationic polymerization and RAFT polymerization.

2. Experimental

2. 1. Materials

Isobutyl vinyl ether (IBVE) (TCI; >99.0%), MOVE (kindly donated by Maruzen Petrochemical; >99.0%), styrene (St) (TCI; >99.0%) was washed with aqueous alkaline solution and then with water. These monomers were distilled twice over calcium hydride and were stored in a brown ampule under dry nitrogen in refrigerator. Ethyl acrylate (EA) (TCI; >99.0%) was purified using inhibitor removers prepac column (Aldrich). NIPAM was recrystallized with benzene/hexane (3/7 v/v) and dried in vacuo. For solvent, toluene (Wako; > 99.5%) was washed by the usual method and then was

distilled over calcium hydride just before use. Ethyl acetate (Wako; >99.5%) as an added base for living cationic polymerization was distilled twice over calcium hydride and was stored in a brown ampule under dry nitrogen. Trifluoroacetic acid (Nacalai; 99.5%) and EtAlCl₂ (Aldrich; 1.0 M ethylaluminum dichloride in hexanes) was used as commercially supplied. The initiator, 2,2'-azobis(isobutyronitrile) (Wako; AIBN) was recrystallized from diethyl ether and stored in refrigerator.

2. 2. *Synthesis of BVCT and BVCT-TFA*

BVCT was prepared as follows: potassium phosphate (46 g, 0.22 mol) and acetone (760 mL) were added into 1 L of round-bottom flask and stirred at room temperature. When white suspension appeared, benzyl mercapton (25.4 mL, 0.22 mol) was added and stirred for 3.5 hours. 39.2 mL of carbon disulfide (0.65 mol) was then added, and after 4 hours, 2-chloroethyl vinyl ether (44 mL, 0.43 mol) was added, and continued to stir for a day. The solution was then filtered and the solvent was removed by evaporation. The resulting liquid was dissolved into 120 mL hexane and washed three times using deionized water (120 mL). The hexane layer was recovered, and followed by adding sodium sulfate or potassium hydroxide and dried overnight. It was then filtered and the excess hexane was removed by evaporator. The product was then isolated from residue by column chromatography, using silica gel as stationary phase, with mixture of ethyl acetate and hexane as eluent (1:15 v/v). The solvent was evaporated to dryness and the product identity was verified using ¹H NMR spectroscopy (yield: 50 %). ¹H NMR (CDCl₃, 25 °C): δ 3.62 (t, 2H, CSCH₂CH₂, *J* = 6.3 Hz), 3.87 (t, 2H, CSCH₂CH₂, *J* = 6.3 Hz), 3.97 and 4.13 (dd, 2H, OCHCH₂, *J* = 6.8 and 2.3 Hz), 4.55 (s, 2H, CSCH₂C₆H₅), 6.35 (q, 1H, OCHCH₂, *J* = 6.8 Hz), 7.18 (m, 5H, CSCH₂C₆H₅). ¹³C NMR (CDCl₃, 25 °C): δ 35.43, 41.55, 65.26 (all CH₂), 87.42 (OCHCH₂), 127.71 (phenyl-C4), 128.60 (phenyl-C3), 129.14 (phenyl-C2), 134.73 (phenyl-C1), 151.05 (OCHCH₂), 222.78 (CS(S)S). IR

(neat, r.t.): 1062 , 1188, 1399 cm^{-1} .

To synthesize BVCT-TFA, the procedure is as follows. BVCT (0.51 g) was added into a Schlenk tube and dried by azeotropic distillation performed in toluene. Then, the solution was diluted to 100 mM in toluene. In another Schlenk tube, toluene (13.8 mL) was added using a dry syringe and trifluoroacetic acid toluene solution was added and diluted to 100 mM. In a round bottom flask, 2 mL of each Schlenk tube were added and stirred for 10 min while cooling to 0 °C. The product identity was verified by ^1H NMR spectroscopy.

2. 3. Cationic Polymerization Procedures

Cationic polymerization was carried out at 0 °C under a dry nitrogen atmosphere in a glass tube equipped with a three-way stopcock baked at 250 °C for 10 min before use. First, BVCT-TFA was diluted to 50 mM in toluene prior to use. Toluene (3.25 mL), ethyl acetate (0.50 mL, 5.1 mmol), IBVE (0.25 mL, 0.095 mmol), and 50 mM of BVCT –TFA in toluene (0.50 mL) were added into the glass tube using dry medical syringes, successively. The polymerization was initiated by the addition of a prechilled 10 mM EtAlCl_2 solution in toluene at 0 °C. This is the procedure for the cationic polymerization in Fig. 2. For a thermoresponsive polymer, MOVE (0.26 mL, 1.0 mmol) was used instead of IBVE as follows: $[\text{MOVE}]_0 = 0.38 \text{ M}$, $[\text{BVCT-TFA}]_0 = 5.0 \text{ mM}$, $[\text{ethyl acetate}] = 1.0 \text{ M}$, $[\text{EtAlCl}_2]_0 = 10 \text{ mM}$. After the desired time, the reaction was terminated with prechilled methanol (0.5 mL) containing a small amount of aqueous ammonia solution (0.1 wt%). The quenched mixture was diluted in either hexane or dichloromethane and was successively washed with 0.1 mol/L hydrochloric acid, water, 0.1 mol/L aqueous NaOH solution, and water to remove the initiator residues. The volatiles were then removed under reduced pressure over 50 °C, and the residue was vacuum-dried for a day at room temperature. The monomer conversion was determined by gravimetry.

When BVCT was used as a comonomer with MOVE for backbone of graft copolymer, the polymerization was conducted as follows: poly(MOVE-*co*-BVCT) was prepared at 0 °C under a dry nitrogen atmosphere in a glass tube equipped with a three-way stopcock baked at 250 °C for 10 min before use. First, BVCT (0.57 g) was added into the first test tube and dried by azeotropic distillation performed in toluene. Then, the solution was diluted to 250 mM in toluene. In a Schlenk tube (A), toluene (8.4 mL), 250 mM of BVCT in toluene (0.75 mL) and 100 mM of trifluoroacetic acid in toluene solution (0.75 mL) were added and stirred for 10 min while cooling to 0 °C. Ethyl acetate (1.5 mL) and MOVE (0.6 mL) were then added to the Schlenk tube (A) using dry medical syringe. 1.5 mL of BVCT solution from the first test tube was added to the Schlenk tube (A) and stirred for 10 min while cooling to 0 °C. In another Schlenk tube (B), toluene (3.6 mL) and EtAlCl₂ in hexane solution (0.4 mL) added and stirred for 10 min while cooling to 0 °C. The polymerization was started when 1.5 mL of this mixture (B) was added to the Schlenk tube (A). After the desired time, the reaction was terminated with prechilled methanol (0.5 mL) containing a small amount of aqueous ammonia solution (0.1 wt%). The quenched mixture was diluted in dichloromethane and was successively washed with 0.1 mol/L hydrochloric acid, water, 0.1 mol/L aqueous NaOH solution, and water to remove the initiator residues. The volatiles were then removed under reduced pressure over 50 °C, and the residue was vacuum-dried for a day at room temperature. The monomer conversion was determined by gravimetry.

2. 3. RAFT Polymerization Procedures

Either poly(IBVE) or poly(MOVE) macro-CTA with various *DP* (degree of polymerization) obtained by living cationic polymerization was mixed with AIBN and varying amount of radically polymerizable monomers such as EA, St, and NIPAM in a Schlenk tube. These are then diluted in toluene for the desired concentration in a Schlenk tube equipped with a magnetic stir bar. For

example, the typical contents for the polymerization of EA are as follows: toluene (3.0 g, 32mmol), EA (0.50 g, 5.3 mmol), poly(IBVE) macro-CTA (0.054 g, 23.5 μmol , $DP = 20$), AIBN (0.87 mg, 5.3 μmol); $[\text{EA}]_0/[\text{poly}(\text{IBVE}) \text{ macro-CTA}]_0/[\text{AIBN}]_0 = 200:1:0.2$ molar ratio. After three freeze-thaw-pump cycles, the flask was filled with nitrogen and sealed. Then, each polymerization was allowed to proceed at 70 °C and quenched after the desired time via cooling in ice water and exposure to air. For block copolymers including poly(IBVE) blocks, the volatiles were then removed under reduced pressure over 40 °C, and the residue was vacuum-dried for a day at room temperature. For poly(MOVE)-*b*-poly(NIPAM), the crude product was then purified by dialysis against deionized water using semipermeable cellulose tubing (SPECTRA/POR, corresponding to a molecular weight cutoff of 1000 Da) with at least six changes of deionized water, followed by lyophilization.

For graft polymerization, the procedure was similar as above. In a round-bottom flask equipped with a magnetic stir bar, macro-CTA (0.62 g, 68.8 μmol), toluene (11.3 g, 0.12 mol), NIPAM (2.1 g, 18.6 mmol), AIBN (2.3 mg, 13.8 μmol) ($[\text{NIPAM}]_0/[\text{poly}(\text{IBVE}) \text{ macro-CTA}]_0/[\text{AIBN}]_0 = 200:1:0.2$ molar ratio) were added and stirred. After three freeze-thaw-pump cycles, the flask was filled with nitrogen and sealed. Then, each polymerization was allowed to proceed at 70 °C and quenched after the desired time via cooling in ice water and exposure to air. The crude product was then purified by dialysis against deionized water using semipermeable cellulose tubing (SPECTRA/POR, corresponding to a molecular weight cutoff of 1000 Da) with at least six changes of deionized water, followed by lyophilization.

2.4 Polymer characterization

Molecular weight distributions (MWDs) excluding those of poly(MOVE)-*b*-poly(NIPAM) were assessed by gel permeation chromatography (GPC) in tetrahydrofuran (THF) at 40 °C using three polystyrene gel columns [TSK gel G-MH_{HR}-M $\times$ 3 (exclusion limit: 4×10^6 (PSt)); 7.8 mm i.d. $\times$

300 mm each; flow rate 1.0 mL/min] connected to a Tosoh CCPMII pump and a RI-8020 and UV-8020 for refractive index (RI) and ultraviolet (UV) detector, respectively. The RI detector was mainly used for determining of number-average molecular weight (M_n) and the polydispersity (M_w/M_n). For poly(MOVE)-*b*-poly(NIPAM), the MWDs were assessed by another GPC in *N,N*-dimethylformamide (DMF) with 10 mM LiBr at 40 °C using a polystyrene gel columns [TSK gel G-MH_{HR}-M $\times$ 2; flow rate 1.0 mL/min] connected to a Tosoh CCPM-II pump and a RI-8012 and UV-8000 for refractive and UV detector, respectively. M_n and M_w/M_n was calculated from GPC curves on the basis of a PSt calibration. The ¹H NMR spectra to determine the detailed structure such as the number-average end functionality of the RAFT terminal (F_n) and the compositions of block copolymers were recorded on either JEOL JNM-EX300 (300 MHz) or JEOL JNM-EX500 spectrometer (500 MHz). Matrix-assisted laser desorption ionization time-of-flight mass (MALDI-TOF-MS) spectra were recorded using a Bruker Daltonics autoflex spectrometer (linear mode) using dithranol as the matrix and sodium trifluoroacetate as the ion source (polymer sample/dithranol/sodium trifluoroacetate = 1/8/1 weight ratio).

2.5 Characterization of Aqueous Block Copolymer Solutions

Aqueous solutions of the copolymers were prepared by dissolving the polymer in Mill-Q water and diluting the sample to those at a desired concentration. The thermoresponsive behavior of the solutions were measured by monitoring the transmittance of a 500 nm light beam through a 1.0 cm glass sample cell at a rate of 1.0 °C/min on heating and cooling scans between 15 and 85 °C. The transmittance was recorded on a JASCO V-500 UV/vis spectrometer equipped with a Peltier-type thermostatic cell holder ETC-505. DSC measurements were performed using a Micro Calorimetry System (MicroCal) at a rate of 1.0 °C/min in heating and cooling scans between 20 and 80 °C. The block copolymer sample dissolved in water (0.5 wt %) was degassed and transferred to the sample

cell (cell volume: 1.22 mL) with a syringe. An identical volume of the solvent of the same composition was placed in the reference cell. Dynamic light scattering (DLS) studies were performed using a DLS-7000 (Photol, Otsuka Electronics) at various temperatures at scattering angle of 90° using 0.1–0.2 wt % aqueous solution of the thermoresponsive poly(MOVE)-*b*-poly(NIPAM) micelles. The light source was a He–Ne laser (10 mW, $\lambda = 632.8$ nm). The intensity-average hydrodynamic diameter (D_h) and polydispersity (PDI, μ_2/I^2) were calculated by cumulants analysis of the experimental correlation function using the attached software of the DLS-7000. Atomic force microscopy (AFM) images were recorded using a dynamic force mode (DFM) at ambient conditions with a SPM-9700 (Shimadzu) scanning probe microscope. Silicon AFM probe tip (Olympus, OMCL-AC160TS-C3) with a radius of 7 nm, a spring constant of 26 N/m, and a resonance frequency of 300 kHz were used. A sample for AFM imaging was prepared at 45 °C by placing a 20 μ L drop of the block copolymer solution (0.05 wt% polymer solution) on freshly cleaved muscovite mica (10 $\times$ 10 mm, V-4 grade, Alliance Biosystems) and allowing it to dry in air at 45 °C for a day.

3. Results and discussion

3.1. Synthesis of BVCT and BVCT-TFA

First, novel vinyl ether, BVCT, was prepared by benzyl mercapton, carbon disulfide, and 2-cholorovinyl ether (50 % yield). The BVCT is vinyl ether, a cationically polymerizable monomer and a RAFT agent, i.e. a trithiocarbonate group with a substituent benzyl group as a free radical leaving group. As illustrated in Scheme 1, poly(vinyl ether)s were synthesized with the use of the adduct of trifluoroacetic acid with BVCT, BVCT-TFA.

Fig. 1 shows ^1H NMR spectra for BVCT and BVCT-TFA. All the signal peaks are exhibited and at 6.5 ppm, the signal peak (**e'**) ascribed for vinyl group at the terminal end is appeared (Fig. 1B),

indicating that BVCT is not self-polymerized and successfully synthesized. By adding trifluoroacetic acid as a protonic acid, this peak is disappeared, and the methylene peak at 3.6 ppm (**e**) confirmed the presence of trifluoroacetic acid (TFA). Furthermore, each characteristic peaks from IR spectrum can be attributed as follows: the strong band of ether group is observed at 1062 cm^{-1} . Also, C=S stretching frequency for trithiocarbonate group is also appeared at 1188 cm^{-1} and C=C band from ester groups is shown at 1399 cm^{-1} , respectively. BVCT is yielded more than 50 % and thus quantitatively synthesized.

Fig. 1. ^1H NMR spectra of (A) BVCT-TFA and (B) BVCT in CDCl_3 at 25 $^\circ\text{C}$.

3.2. Living cationic polymerization of vinyl ether from BVCT-TFA

Using BVCT-TFA/ EtAlCl_2 /ethyl acetate initiating system, poly(IBVE) was prepared as a typical example. Fig. 2A shows the representative time-conversion curves and the first-order kinetic plots

for the polymerization of IBVE. Although there is the RAFT moiety in the initiator BVCT-TFA, the initiating system induced a quantitative polymerization without an induction phase. The polymerization rate was first order with respect to monomer concentration, as evidenced by linear plots of logarithmic conversion data, $\ln([M]_0/[M])$, against time, where $[M]_0$ and $[M]$ are monomer concentration at 0 and a certain time, respectively. The polymerization was relatively slow (conversion 66.5 % at 4h). Fig. 2B shows the M_n and the M_w/M_n values of the product polymers. The M_n increased in a direct proportion to the monomer conversion and is close to the calculated values assuming that one polymer chain form per one molecule of the BVCT-TFA. The typical GPC curves are shown in Fig. 2C. The poly(IBVE) obtained also had relatively narrow M_w/M_n and shifted to higher molecular weight as conversion increased. Fig. 3 shows ^1H NMR spectrum of the resulting poly(IBVE). The polymer exhibited the signals ascribed to the BVCT (**a-f**) (i.e., α -end), protons due to IBVE repeating units (**h-k**) and ω -end (**m**). Furthermore, peaks **a** and **b** of the leaving group are seen in poly(IBVE). This indicates that the poly(IBVE) possesses the RAFT polymerization moiety, i.e. free radical leaving group (benzyl group) and a trithiocarbonate group. This result indicates that these groups for RAFT polymerization were stable during living cationic polymerization process. The number average end functionality (F_n) was determined from the peak intensity ratio of the α -end group **a** or **b** to the ω -end group **m**. The F_n of the α -end group is 0.90 assuming that all the ω -end groups are methoxy group.

Fig. 2. Living cationic polymerization of IBVE using BVCT-TFA in toluene at 0 °C: $[IBVE]_0 = 0.38$ M, $[BVCT-TFA]_0 = 5.0$ mM, $[EtAlCl_2]_0 = 10$ mM, $[ethyl\ acetate] = 1.0$ M. (A) Kinetic plots, (B) M_n and M_w/M_n as a function of monomer conversion, and (C) typical GPC curves (THF eluent, RI).

Fig. 3. Typical 1H NMR spectrum of poly(IBVE) macro-CTA (entry 2) in $CDCl_3$ at 25 °C.

Next, MALDI-TOF-MS spectroscopy analysis for the poly(IBVE) macro-CTA was conducted in order to analyze both terminal end structures (α and ω -ends). The estimated chemical structures for each peak are also summarized in Fig. 4 in detail. The spectrum exhibited two major peaks (filled circle in red and blue), in which each peak is separated by 100 mass units, corresponding to the molar mass of IBVE repeating unit. For example, the peak **a** value is consistent with the calculated mass of poly(IBVE) with BVCT α -end and methoxy ω -end; where, the experimental signal (2128.1 g/mol) fits the calculated molecular weight with Na^+ (2128.4 g/mol). Meanwhile, the peak **b** is ascribed to poly(IBVE) initiated by proton, derived from an adventitious water or an excess TFA (1858.0 g/mol, $n = 18$). On the basis of these results, the α -end-functionality is calculated to be approximately 90%, which is in good agreement with $F_n = 0.90$ calculated from ^1H NMR spectroscopy. This functionality of RAFT moiety is sufficient for the following block copolymerization, larger than that of previous “counteranion recovery” method (ca. 0.8) [14,15].

3.3. Synthesis of various block copolymers via RAFT polymerization

After macro-CTA was obtained, RAFT polymerizations [26,27] were conducted using several types of radically monomers. Some monomers were chosen appropriately based on the structure of RAFT agent that was reported by many researchers [28]. Table 1 shows results of block copolymerization of EA, St, and NIPAM via RAFT polymerization. However, methyl methacrylate and vinyl acetate were not polymerized from these macro-CTA of poly(IBVE) and poly(MOVE).

Table 1

Synthesis of various block copolymers via RAFT polymerization^a

Entry	Polymer structure ^b	$M_n \times 10^{-3c}$	M_w/M_n^c
		Macro-CTA / Block	Macro-CTA / Block
1	IBVE ₂₁ - <i>b</i> -EA ₁₅₂	1.7 / 17.3	1.24 / 1.29
2	IBVE ₃₄ - <i>b</i> -EA ₁₃₈	2.2 / 21.1	1.20 / 1.26
3	MOVE ₆₆ - <i>b</i> -EA ₉₃	5.0 / 27.8	1.27 / 1.32
4	IBVE ₄₂ - <i>b</i> -NIPAM ₁₉₇	4.8 / 24.7	1.18 / 1.37
5	MOVE ₆₁ - <i>b</i> -NIPAM ₁₅₀	7.5 / 19.9	1.29 / 1.33
6	IBVE ₁₆ - <i>b</i> -St ₇₄	1.2 / 3.0	1.24 / 1.53
7	IBVE ₄₂ - <i>b</i> -St ₂₈	4.8 / 7.6	1.18 / 1.44
8	MOVE ₆₆ - <i>b</i> -St ₃₅	5.3 / 8.8	1.33 / 1.45

^a RAFT polymerization condition: [monomer]₀: [macro-CTA]₀: [AIBN]₀ = 200:1:0.2, [monomer]₀ = 15 wt% in toluene at 70 °C. The macro-CTAs were synthesized by living cationic polymerization using BVCT-TFA/EtAlCl₂/ethyl acetate initiating system.

^b The segment *DP* in the formula was determined by ¹H NMR spectroscopy on the basis of *DP* of the macro-CTA assuming that *F_n* = 1.0 of α-end.

^c Determined by GPC (PSt calib.)

The RAFT polymerization of EA using poly(IBVE) macro-CTA was conducted in toluene at 70 °C with molar ratio [EA]₀/[poly(IBVE)]₀/[AIBN]₀ = 200:1:0.2. Fig. 5A shows kinetic curve for RAFT polymerization of EA. The polymerization shows a long induction period about 2h due to slow cross-initiation of EA by the benzyl radical from the macro-RAFT agent and possibly unfunctionalized PIBVE precursor. After the induction period, the polymerization proceeded and

shows a linear first order plot. From Fig. 5B, the average number of molecular weight increased linearly with conversion and the molecular weight distribution were relatively narrow except the polymer at the low conversion. The molecular weight distribution clearly shifted toward the higher molecular weights relative to that of poly(IBVE) macro-CTA (Fig. 5C). The tailing of poly(IBVE) was seen like a shoulder peak, indicating that macro-CTA was contained a little of poly(IBVE) initiated by water about 10%. This is agreed with the MALDI-TOF-MS result and the CTA efficiency. The block copolymer, $\text{MOVE}_{66}\text{-}b\text{-EA}_{93}$ (entry 3), prepared using poly(MOVE) macro-CTA was also obtained under the same condition using poly(IBVE) macro-CTA ($M_n = 27.8 \times 10^3$, $M_w/M_n = 1.33$). No differences were seen when either poly(MOVE) macro-CTA or poly(IBVE) macro-CTA was used.

Fig. 5. RAFT polymerization of EA using poly(IBVE) macro-CTA (entry 1) in toluene at 70 °C: $[\text{EA}]_0/[\text{poly}(\text{IBVE})]_0/[\text{AIBN}]_0 = 200:1:0.3$, $[\text{EA}]_0 = 15$ wt%. (A) Kinetic plots, (B) evaluation of M_n (○) and M_w/M_n (●) with conversion, and (C) the typical GPC curves for poly(IBVE) macro-CTA and

poly(IBVE)-*b*-poly(EA) at 5 and 8 h.

The block copolymerization of St and NIPAM was also conducted under the same condition. Both MWDs clearly shifted toward higher molecular weights relative to the M_n of both poly(IBVE) macro-CTA and poly(MOVE) macro-CTA and the RAFT polymerizations exhibited linear first-order plots, indicating an approximately constant number of growing species as well as the MWDs of EA as shown in Table 1. Intriguingly, double thermo-responsive block copolymer, poly(MOVE)-*b*-poly(NIPAM), was also obtained. The polymerization occurred after induction period for 1 hour and the molecular weight distributions are shifted toward higher molecular weight relative to that of poly(MOVE) macro-CTA, and the molecular weight distributions are relatively narrow even after block copolymerization.

Fig. 6. RAFT polymerization of NIPAM using poly(MOVE) macro-CTA (entry 5) in toluene at 70 °C: $[NIPAM]_0/[poly(MOVE)]_0/[AIBN]_0 = 200:1:0.3$, $[NIPAM]_0 = 15$ wt%. (A) Kinetic plots, (B) evaluation of M_n (○) and M_w/M_n (●) with conversion, and (C) the typical GPC curves for poly(MOVE) macro-CTA and poly(MOVE)-*b*-poly(NIPAM) at 75 and 90 min.

To confirm the block copolymerization in detail, the ^1H NMR spectrum of a $\text{MOVE}_{61}\text{-}b\text{-NIPAM}_{150}$ (entry 5) was recorded in D_2O at various temperatures. The spectra are depicted in Fig. 7 to investigate the temperature dependence of phase-separation behavior. At 25 $^\circ\text{C}$, which is under T_{ps} of both of poly(NIPAM) (ca. 32 $^\circ\text{C}$) and poly(MOVE) (ca. 66 $^\circ\text{C}$), all peaks of both poly(MOVE) and poly(NIPAM) are appeared. When the temperature is at 45 $^\circ\text{C}$, between T_{ps} 's of poly(NIPAM) and poly(MOVE) homopolymer, all the signals of poly(NIPAM) chain were disappeared, whereas the signal assigned to poly(MOVE) chains remained sharp. Thus, this indicates that self-assemblies like poly(NIPAM)-core micelles are formed at this temperature. This resulting self-assemblies like micelle was reversible, depending on the solution temperature over these temperature ranges.

Fig. 7. Typical ^1H NMR spectra recorded for 1.0 wt % $\text{MOVE}_{61}\text{-}b\text{-NIPAM}_{150}$ (entry 5) in D_2O at (A) 25 $^\circ\text{C}$ and (B) 40 $^\circ\text{C}$. The inset shows the chemical structure of the diblock copolymer with full peak assignments.

3.4. Aqueous solution of poly(MOVE)-*b*-poly(NIPAM)

Fig. 8 show dynamic light scattering (DLS) and DSC thermogram results for poly(MOVE)-*b*-poly(NIPAM) in water. Below 32 °C, the block copolymer is molecularly dissolved and the hydrodynamic diameter (D_h) is below 15 nm with relatively high polydispersity index (PDI) (μ_2/I^2). Above 32 °C, the solution was changed from transparent to slightly opaque evidenced by the decreasing of transmittance at 500 nm as shown in Fig. 8B, indicating micellar solution characteristics. The diameter increased, whereas the PDI decreased with the increasing temperature. The diameter reached about 180 nm at 34 °C. Further increased temperature up to 64 °C induced precipitation due to the both T_{ps} 's of poly(NIPAM) and poly(MOVE).

The relationship between temperature and diameter is also clarified in DSC thermogram and the temperature dependence of the absorbance at 500 nm (0.1 wt%) (Fig. 8B). The results of both measurements indicated that two-step transitions occurred when the block polymer was heated above T_{ps} 's of poly(NIPAM) and poly(MOVE) blocks. The transition temperatures, i.e. 32 °C and 64 °C, were occurred, in agreement to the T_{ps} of poly(NIPAM) and the temperature slightly shifted to low temperature against that of poly(MOVE), respectively. This temperature shift is due to hydrophobic effects of poly(NIPAM) in micellar core.

AFM was also used to confirm the micelle formation. AFM image of micelles deposited on the mica substrate from MOVE₆₁-*b*-NIPAM₁₅₀ diluted solutions (0.05 wt%) at 45 °C are shown in Fig. 9. Spherical micelles and clusters of micelles can be clearly seen in the image. From these observations, it can be concluded that the block copolymer was successfully obtained.

Fig. 8. (A) Variation of hydrodynamic diameter (D_h) and PDI (μ_2/Γ^2) with temperature for MOVE_{61} - b -NIPAM $_{150}$ (entry 5) in water. (B) Temperature dependence of the transmittance (%) at 500 nm (0.1 wt%) and DSC thermogram (0.5 wt %) of aqueous solution of MOVE_{61} - b -NIPAM $_{150}$: heating and cooling rate 1.0 °C/min, heating (—) and cooling (···). The inset values are transition temperatures (peak tops; T_1 and T_2) and their heats of transition (ΔH_1 and ΔH_2).

Fig. 9. AFM (height) images ($5 \times 5 \mu\text{m}$) of $\text{MOVE}_{61}\text{-}b\text{-NIPAM}_{150}$ (entry 5) in water at 45°C deposited onto mica.

3.5. Synthesis of *poly(MOVE-co-BVCT)-g-poly(NIPAM)*

As we mentioned above, BVCT is not only functioned as initiator but also could be used as monomer. MOVE and BVCT copolymer was synthesized via living cationic polymerization under the same condition (see Table 2). Fig. 10 shows representative ^1H NMR spectrum for *poly(MOVE-co-BVCT)*. Fig. 11 shows the typical GPC results for *poly(MOVE-co-BVCT)*. For ^1H NMR spectroscopy result, all peaks were attributed to MOVE (**g-k**) and BVCT units (**a-f**). Furthermore, the existence of the RAFT terminal group was confirmed by UV detector in GPC measurement at 308 nm, which also detected at the same position as RI detection. The 308 nm wavelength is the maximum absorption wavelength of $\pi\text{-}\pi^*$ absorption bands of the trithiocarbonate group. The resulting *poly(MOVE-co-BVCT)* was also monodisperse, indicating that the BVCT can be functioned as a monomer. However, the relative reactivities for MOVE and BVCT were determined by Kelen-Tüdös method, giving values of 0.25 ± 0.16 (r_{MOVE}) and 1.3 ± 0.045 (r_{BVCT}),

respectively [29]. These values show that BVCT is more reactive than MOVE due to the structure of MOVE with an ether bond in the pendant to stabilize the propagating carbocation. Thus, this indicates that the sequence distribution of the product copolymer is not perfectly random.

Using the poly(MOVE-*co*-BVCT) as a backbone, the graft copolymerization of poly(NIPAM) was investigated. Table 2 shows the polymerization result. Regardless of the *DP* for poly(MOVE-*co*-BVCT), all of the polymerization smoothly progressed as that of block copolymerization. From typical GPC results in Fig. 11, MWD of graft copolymer, poly(MOVE-*co*-BVCT)-*g*-poly(NIPAM), was slightly shifted to higher molecular weights relative to that of the corresponding poly(MOVE-*co*-NIPAM) backbone. This result is different to those of linear block copolymer, where the MWD of the polymer is considerably shifted. This is due to compact size in eluent of GPC relative to the block copolymer. Furthermore, the existence of the RAFT terminal group at 308 nm shows that BVCT is not decomposed from the backbone. Moreover, the graft copolymer also exhibited the thermoresponsiveness (precipitation) above T_{ps} of poly(NIPAM) homopolymer. No micelle formed in water above T_{ps} of poly(NIPAM) graft chain unlike the case of block copolymers for (MOVE_{*n*}-*co*-BVCT_{*m*})-*g*-NIPAM_{*x*} (*n* = 62-73, *m* = 1-9, *x* = 19-214). This is due to the polymer structure in which the T_{ps} of graft chain is lower than that of backbone. In short, the obtained graft polymer is more hydrophobic than that of the block copolymer, and it is difficult for poly(NIPAM) grafts to stabilize the aggregates.

Fig. 10. Typical ^1H NMR spectra recorded for $\text{MOVE}_{62}\text{-co-BVCT}_9$ in CDCl_3 at 25 °C. Asterisks denote solvent peaks.

Table 2.

Graft copolymers, poly(MOVE-co-BVCT)-g-poly(NIPAM), i.e.

$\text{BVCT-}[(\text{MOVE}_n\text{-co-BVCT}_m)\text{-g-NIPAM}_x]$ obtained from RAFT polymerization using poly(MOVE-co-BVCT) backbone^a

Entry	Resulting polymer structure ^b	$M_n \times 10^{-3}$ (GPC) ^c backbone ^d / graft ^e	M_w/M_n (GPC) ^c backbone ^d / graft ^e
9	$(\text{MOVE}_{73}\text{-co-BVCT}_1)\text{-g-NIPAM}_{93}$	7.6 / 14.0	1.30 / 1.54
10	$(\text{MOVE}_{73}\text{-co-BVCT}_1)\text{-g-NIPAM}_{214}$	7.6 / 25.4	1.30 / 1.72
11	$(\text{MOVE}_{72}\text{-co-BVCT}_2)\text{-g-NIPAM}_{46}$	7.1 / 10.0	1.31 / 1.42
12	$(\text{MOVE}_{72}\text{-co-BVCT}_2)\text{-g-NIPAM}_{126}$	7.1 / 18.1	1.31 / 1.45
13	$(\text{MOVE}_{69}\text{-co-BVCT}_3)\text{-g-NIPAM}_{29}$	7.4 / 9.1	1.38 / 1.43
14	$(\text{MOVE}_{69}\text{-co-BVCT}_3)\text{-g-NIPAM}_{70}$	7.4 / 13.8	1.38 / 1.41
15	$(\text{MOVE}_{62}\text{-co-BVCT}_9)\text{-g-NIPAM}_{19}$	6.5 / 9.2	1.33 / 1.38

^aRAFT polymerization: $[\text{monomer}]_0:[\text{backbone}]_0:[\text{AIBN}]_0 = \text{X}:1:0.2$ (X is close to DP of poly(NIPAM) in Table; X = 180, 440, 143, 375, 120, 260, 222 for entry 9-15, respectively. All conv ~ 100%), $[\text{monomer}]_0 = 15$ wt% in toluene at 70 °C.

^bThe segment DP in the formula was determined by ^1H NMR spectroscopy. All backbones include BVCT α -endgroup because of BVCT-TFA initiator for living cationic polymerization. For example, in the case of entry 9, two BVCT monomers were utilized to prepare the backbone.

^cDetermined by GPC (PSt calib.).

^dLiving cationic polymerization: $[\text{monomers}]_0 = 0.35$ M (monomers: MOVE and BVCT), $[\text{BVCT-TFA}]_0 = 5$ mM, $[\text{EtAlCl}_2]_0 = 10$ mM, $[\text{ethyl acetate}] = 1.0$ mM.

^eMonomer reactivity for synthesis of backbone: $r_{\text{MOVE}} = 0.25 \pm 0.16$, $r_{\text{BVCT}} = 1.3 \pm 0.045$.

Fig. 11. Typical GPC curves for $\text{MOVE}_{69}\text{-co-BVCT}_3$ and $(\text{MOVE}_{69}\text{-co-BVCT}_3)\text{-g-NIPAM}_{29}$, respectively. Line and dotted curves are detected by RI and UV at 308 nm, respectively.

4. Conclusion

In conclusion, novel block and graft copolymers were synthesized using a novel vinyl ether-type RAFT agent, BVCT, which possesses trithiocarbonate and benzyl group for RAFT polymerization via the combination of living cationic polymerization of vinyl ethers and RAFT polymerization. For block copolymers, the novel BVCT-TFA play an important role to produce well-defined block copolymers, which is both a cationogen under EtAlCl_2 initiation system in the presence of ethyl acetate for living cationic polymerization and a RAFT agent. Since the BVCT-TFA was utilized as an initiator, the resulting polymer, poly(vinyl ether)s, by living cationic polymerization had a high number average α -end functionality (≥ 0.9) because the BVCT-TFA is the cationogen for living cationic polymerization. In addition, this α -end group was not decomposed during polymerization.

These are determined by both ^1H NMR and MALDI-TOF-MS spectrometry in detail. Furthermore, this poly(vinyl ether)s worked well as a macromolecular chain transfer agent for RAFT polymerization. The RAFT polymerization of radically polymerizable monomers was conducted in toluene using 2,2'-azobis(isobutyronitrile) at 70 °C. As an evidence of the successful block copolymerization, double thermoresponsive block copolymers poly(MOVE)-*b*-poly(NIPAM) were synthesized. The product block copolymers reversibly formed and deformed micellar assemblies above the T_{ps} of poly(NIPAM) block in water. In preparing the graft copolymer via the combination of living cationic polymerization and RAFT polymerization, this BVCT acted as a comonomer for living cationic polymerization. When BVCT was copolymerized with MOVE by living cationic polymerization, the relative reactivities for MOVE and BVCT were 0.25 ± 0.16 (r_{MOVE}) and 1.3 ± 0.045 (r_{BVCT}), respectively. Using this copolymer, graft copolymerization with NIPAM via RAFT polymerization was conducted, and well-defined poly(MOVE-*co*-BVCT)-*g*-poly(NIPAM) was successfully obtained. However, since the obtained graft polymer is more hydrophobic than that of the block copolymer, no micelle formed in water above T_{ps} of poly(NIPAM) graft chain unlike the case of block copolymer.

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Appendix A. Supplemental data

Supplementary data related to this article can be found.

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TITLE

Synthesis of thermoresponsive block and graft copolymers via the combination of living cationic polymerization and RAFT polymerization using a vinyl ether-type RAFT agent

GRAPHICAL ABSTRACT FIGURE