

## NOTE

# RAFT homopolymerization of vinylbenzyl chloride with benzyl ethyl trithiocarbonate and synthesis of block copolymers from poly(VBC) macro-RAFT agent and *N*-isopropylacrylamide

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## INTRODUCTION

Poly(vinylbenzyl chloride) (PVBC) is an important polymer that has a reactive benzyl chloride group and is thus easily converted to various functional polymers.<sup>1</sup> Radical polymerization is one of the most widely used processes for commercial production of vinyl polymers. Conventional radical polymerization, however, severely limits the control of molecular-weight distribution, copolymer composition and molecular architecture. To remedy these problems, many living radical polymerization methods, such as nitroxide-mediated polymerization, atom transfer radical polymerization and reversible addition-fragmentation chain transfer (RAFT), have been developed.<sup>2,3</sup>

Living radical polymerizations were applied to the polymerization of vinylbenzyl chloride (VBC) to obtain the well-defined PVBC polymer. However, the atom transfer radical polymerization of VBC yielded hyperbranched polymers because benzylic chloride acts as an inimer.<sup>4</sup> In addition, PVBCs with high polydispersity indices were produced by nitroxide-mediated polymerization with 2,2,6,6-tetramethyl-1-piperidinyloxy because of radical transfer to chloromethyl groups, accompanied by the formation of the hydroxylamine of 2,2,6,6-tetramethyl-1-piperidinyloxy and/or the corresponding oxoammonium chloride that can initiate new controlled PVBC chains.<sup>5</sup> However, most RAFT polymerizations of VBC have been performed for the synthesis of copolymers with styrene, whereas few studies have dealt with the homopolymerization of VBC. Among them, ABA and BAB triblock copolymers of VBC and styrene with low dispersity were prepared by RAFT polymerization using a symmetrical trithiocarbonate, butan-1,4-diyl-bis(1-phenylethyl)trithiocarbonate, as the RAFT agent.<sup>6</sup>

Quite recently, Ameduri *et al.* also studied the kinetics of RAFT polymerization of VBC in the presence of xanthate or

trithiocarbonate and found that RAFT polymerization in the presence of *O*-ethyl-*S*-(1-methyloxycarbonyl)ethyl xanthate or dibenzyl trithiocarbonate yielded polymers with a broad molecular distribution and relatively narrow molecular distribution, respectively. However, even in the latter polymerization, the polydispersity increased to approximately 1.6 when the conversions reached approximately 60%.<sup>7</sup> Moreover, when the symmetrical trithiocarbonate, dibenzyl trithiocarbonate, is used as the RAFT agent, the resulting polymers contain trithiocarbonate groups in the center of the main chains that react with various nucleophiles and result in a decrease in the molecular weights of the polymers. Therefore, a more suitable synthetic method to prepare controlled PVBC is required.

In this study, we report the successful RAFT polymerization of VBC with a trithiocarbonate unit at the chain end of the polymer. PVBC with controlled molecular weight and polydispersity was obtained by using benzyl ethyl trithiocarbonate (BET) as the RAFT agent. Furthermore, successful application of this method to the synthesis of block copolymers from the PVBC macro-RAFT agent and *N*-isopropylacrylamide (NIPAM) is also described. PNIPAM shows characteristic thermal responsibility, and introduction of a PNIPAM segment to PVBC can provide a wide variety of applications.

## EXPERIMENTAL PROCEDURE

### Materials

2,2'-Azobis(isobutyronitrile) (AIBN, Tokyo Kasei Kogyo (TCI), Tokyo, Japan, 99.8%) was purified by recrystallization from methanol. VBC (TCI, >90%) was dried using anhydrous MgSO<sub>4</sub> and further purified by vacuum distillation. *N*-Isopropylacrylamide (NIPAM, Wako Chemical Industries (Wako), Osaka, Japan, 98.0%) was purified by recrystallization from *n*-hexane/CHCl<sub>3</sub> (5:1, v/v). Ethanethiol (TCI, >98.0%), carbon disulfide (TCI, >98.0%) and benzyl bromide (TCI, >98.0%) were used without further purification.

The purification of sodium hydride (NaH, 60%, dispersion in paraffin liquid, (TCI) was conducted by washing with hexane. Tetrahydrofuran (stabilizer-free THF (Wako, 99.5%) and toluene (Wako, 98.0%) were used without further purification.

### Synthesis of BET as RAFT agent

Ethaneethiol (1.10 ml, 0.015 mol) was added slowly to a suspension of NaH (0.450 g, 0.019 mol) in dry THF (10 ml) cooled in an ice bath under N<sub>2</sub>, and the mixture was stirred for 1 h at this temperature. CS<sub>2</sub> (2.0 ml, 0.033 mol) was then added, and the mixture was stirred for 1 h. After removal of THF and unconverted CS<sub>2</sub> under reduced pressure, the residue was dissolved in THF (10 ml), and benzyl bromide (1.20 ml, 0.010 mol) was added dropwise at room temperature. The reaction mixture was stirred overnight, and the reaction was quenched by adding water. The organic solvents were removed under reduced pressure. The residue was diluted with *n*-hexane, and the organic phase was separated. The aqueous phase was extracted with *n*-hexane three times. The combined organic layer was dried over MgSO<sub>4</sub>, filtered and evaporated under vacuum, yielding a light yellow liquid. The yield was 1.80 g (80%).

Fourier-transform infrared (FT-IR; KBr,  $\nu$ , cm<sup>-1</sup>): 2953 (C-H, aliphatic), 2895 (C-H, aliphatic), 1600 (C=C, aromatic). <sup>1</sup>H nuclear magnetic resonance (NMR; CDCl<sub>3</sub>):  $\delta$  = 7.30 (m, 5H, -C<sub>6</sub>H<sub>5</sub>), 4.61 (s, 2H, Ph-CH<sub>2</sub>-S-), 3.37 (q, 2H, -S-CH<sub>2</sub>-CH<sub>3</sub>), 1.35 (t, 3H, -S-CH<sub>2</sub>-CH<sub>3</sub>).

### Synthesis of PVBC

All polymerizations were performed with AIBN as the radical initiator in degassed sealed tubes. The following is a representative example. BET (45.6 mg, 0.20 mmol), VBC (3.00 g, 19.7 mmol) and AIBN (8.50 mg, 0.050 mmol) were placed in a dry glass ampoule equipped with a magnetic stirring bar, and then the solution was degassed by three evacuate-thaw cycles. After the ampoule was flame-sealed under vacuum, it was stirred at 70 °C for 8 h. The reaction was terminated by rapid cooling with liquid nitrogen. For the determination of monomer conversion, an aliquot of the sample was collected, and the <sup>1</sup>H NMR spectrum was measured in CDCl<sub>3</sub> at room temperature. Monomer conversion determined by the method was 59.3%. The polymerization solution was poured into methanol, and the precipitate was collected by filtration with a membrane filter (Millipore LAMPO 4700 pore size 0.20  $\mu$ m, Millipore, Billerica, MA, USA) and dried *in vacuo* at room temperature overnight to yield light yellow solids. The yield was 1.55 g (50.9%).

FT-IR (KBr,  $\nu$ , cm<sup>-1</sup>): 2923 (C-H, aliphatic), 2850 (C-H<sub>3</sub>), 1600 (C=C, aromatic), 1262 (CH<sub>2</sub>-Cl). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 7.43-6.32 (4H, phenyl group), 4.52-4.31 (2H, benzyl group), 2.49-1.32 (3H, in the main chain), 3.41-3.39 (0.05H, S-CH<sub>2</sub>-CH<sub>3</sub> in the end group).

### Synthesis of block copolymer PVBC-*b*-PNIPAM

The following is a representative example of the synthesis of block copolymers from VBC and NIPAM. The trithiocarbonate-terminated PVBC (0.30 g, 0.043 mmol), NIPAM (0.97 g, 8.61 mmol), AIBN (1.8 mg, 0.011 mmol) and dimethylformamide (8.6 ml) were placed in a dry glass ampoule equipped with a magnetic stirring bar, and then the solution was degassed by three evacuate-thaw cycles. The ampoule was flame-sealed under vacuum and then stirred at 60 °C for 24 h. The polymerization was terminated by rapid cooling with liquid nitrogen. Monomer conversion as determined by <sup>1</sup>H NMR spectroscopy was

78.9%. The crude polymer was purified by re-precipitation into a large excess of diethyl ether. The yield was 0.67 g (52.2%).

The copolymer composition was determined with <sup>1</sup>H NMR spectroscopy by a comparison of peaks associated with the two comonomers. The peaks at 4.52-4.31 and 3.92-4.21 p.p.m., attributed to the benzyl protons of the PVBC and the methine protons of the PNIPAM, respectively, were used for confirmation.

### Measurements

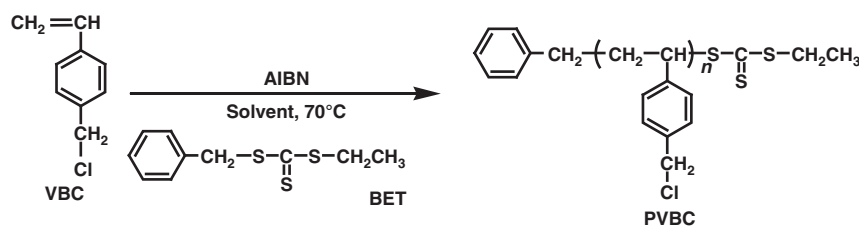
<sup>1</sup>H NMR spectra (500 and 600 MHz) were recorded on JEOL JNM-ECA-500 and JNM-ECA-600 spectrometers (JEOL Ltd., Tokyo, Japan) with chloroform-*d* (CDCl<sub>3</sub>) as the solvent. The chemical shift reference was tetramethylsilane (TMS, 0.00 p.p.m.). FT-IR spectra were measured with a JASCO FT/IR-4100 instrument (4000-400 cm<sup>-1</sup> at 4 cm<sup>-1</sup> resolution). The number-average molecular weight (*M*<sub>n</sub>) and molecular weight distribution *M*<sub>w</sub>/*M*<sub>n</sub> of the PVBC polymers were measured with a TOSOH HLC-8020 size-exclusion chromatography (SEC) unit (TOSOH, Tokyo, Japan; eluent: tetrahydrofuran (THF); calibration: polystyrene) using two TSK gel columns (2 × Multipore H<sub>xl</sub>-M). The number-average molecular weight (*M*<sub>n</sub>) and molecular weight distribution *M*<sub>w</sub>/*M*<sub>n</sub> of the block copolymers were measured with a TOSOH HLC-8220 SEC unit (eluent: dimethylformamide containing 10 mM LiBr as the eluent; calibration: polystyrene) using one gel column (Shodex Asahipak GF-310, Shodex, Tokyo, Japan).

## RESULTS AND DISCUSSION

### RAFT homopolymerization of VBC with BET

One of the key features of RAFT polymerization is the trithiocarbonate group retained at the end of the polymer that is responsible for the living character of RAFT polymerization. Therefore, the choice of RAFT agent is important for the controlled polymerization of vinyl monomers.<sup>8,9</sup> In the RAFT polymerization of VBC, the side reactions originate from the reactive benzyl chloride groups and radical species as described above. The selection of the RAFT agent (R-S-(C=S)-Z) for a particular monomer is extremely important in controlled polymerization,<sup>10,11</sup> requiring fast rates for both addition of a given radical species to the C=S double bond and fragmentation of the intermediate radical species, relative to the rate of propagation. When the Z species has a stabilizing effect on the intermediate radical, fast addition rates can be achieved. The R group must be a good free radical leaving group and efficient at reinitiating polymerization. In this study, we selected BET as the RAFT agent because terminal ethylthio group species are poor radical leaving groups compared to the terminal benzylthio species derived from dibenzyl trithiocarbonate.<sup>7</sup> Thus, the control of radicals produced from fragmentation reactions would be easier, and a trithiocarbonate unit is placed at the chain end of the resulting polymer.

RAFT polymerization of VBC was performed in both solution and bulk states using BET as the RAFT agent. A solution polymerization is conducted in toluene (1 mol/l) at 80 °C, using a constant molar ratio (0.05:50) of VBC to AIBN (Scheme 1). The polymerization proceeded

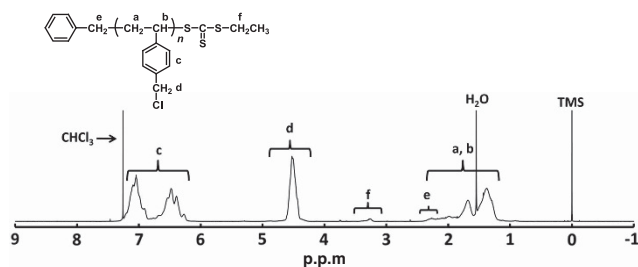


**Scheme 1** Reversible addition-fragmentation chain transfer (RAFT) polymerization of vinylbenzyl chloride (VBC) with benzyl ethyl trithiocarbonate (BET) as a RAFT agent. AIBN, azobis(isobutyronitrile).

homogeneously with a slight increase in the viscosity with polymerization time. After 24 or 48 h, the polymerization solution was poured into methanol. The results are summarized in Supplementary Table 1. The conversions of VBC in solution polymerizations were not very high even after 48 h, so bulk polymerization was performed for 24 h, resulting in moderate conversion (54.6%) of VBC. To improve the conversion of VBC, the molar ratio of AIBN/VBC was increased from 0.05:50 to 0.25:50. The conversion of VBC reached 78.5% in 8 h as expected, and the calculated number-average molecular weight ( $M_n$ ) is the same as the  $M_n$  (6200) determined by SEC using a polystyrene standard. Furthermore, its polydispersity index (PDI) is relatively narrow (1.37).

The structure of the PVBCs was characterized by FT-IR and  $^1\text{H}$  NMR spectroscopy. The FT-IR spectra of the polymers contained characteristic absorptions of the phenyl ring and C-Cl stretching vibration at 1601 and 1265  $\text{cm}^{-1}$ , respectively. Figure 1 shows the  $^1\text{H}$  NMR spectrum of PVBC in  $\text{CDCl}_3$ . Phenyl (c) and chloromethyl (d) protons were clearly observed at 7.42–6.04 and 4.61–4.20 p.p.m., respectively. Furthermore, benzyl (e) and methylene (f) protons adjacent to the trithiocarbonate group derived from BET were also observed at 2.31 and 3.41 p.p.m., respectively.

Based on these preliminary optimization studies, the relationship of  $M_n$  and PDI in the conversion of VBC was studied. The polymerizations were performed with a molar ratio of  $[\text{AIBN}]_0$ : $[\text{BET}]_0$ : $[\text{VBC}]_0 = 0.25$ :1:100 at 70 °C. The results are summarized in Table 1. The  $M_n$  values of PVBC were determined from the integration ratios of methylene protons (f) derived from BET and chloromethyl proton peaks (d). The  $M_n$  and PDI are plotted with the conversion of VBC (Figure 2).  $M_n$  linearly increases with conversion, and the PDIs remain relatively low. These results



**Figure 1** The  $^1\text{H}$  nuclear magnetic resonance spectrum (500 MHz, in  $\text{CDCl}_3$ ) of poly(vinylbenzyl chloride). TMS, Tetramethylsilane.

**Table 1** RAFT polymerization of VBC in the presence of BET<sup>a</sup>

No.	Time (h)	Conv <sup>b</sup> (%)	Yield <sup>c</sup> (%)	$M_n$			$M_w/M_n^d$
				Theo. <sup>e</sup>	NMR <sup>f</sup>	SEC <sup>d</sup>	
1	4	50.7	42.6	7600	8000	7700	1.39
2	8	59.3	50.9	9100	8800	8700	1.38
3	12	64.6	63.4	11 200	10 100	10 300	1.30
4	24	80.5	80.2	13 700	13 900	11 800	1.32

Abbreviations: AIBN, azobis(isobutyronitrile); NMR, nuclear magnetic resonance; RAFT, reversible addition-fragmentation chain transfer; SEC, size-exclusion chromatography; Theo., theoretical; VBC, vinylbenzyl chloride.

<sup>a</sup> $[\text{AIBN}]_0$ : $[\text{BET}]_0$ : $[\text{VBC}]_0 = 0.25$ :1:100 at 70 °C under bulk condition.

<sup>b</sup>Conversion determined by  $^1\text{H}$ -NMR analysis of the crude product.

<sup>c</sup>Insoluble parts in methanol.

<sup>d</sup>Determined by SEC based on polystyrene standards (eluent: THF).

<sup>e</sup>The theoretical  $M_n$  values were calculated on the basis of the conversion of styrene.

<sup>f</sup>The  $M_n$  values were calculated by end-group analysis (after reprecipitation).

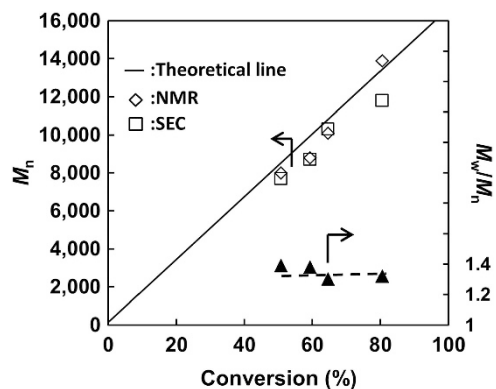
indicate that the RAFT polymerizations of VBC using BET as the RAFT agent proceed smoothly and yield the desired controlled PVBC even in high conversion, demonstrating the need for a judicious choice of the RAFT agent to achieve good control of RAFT polymerizations.

### Synthesis of block copolymer from PVBC macro-RAFT agent and NIPAM

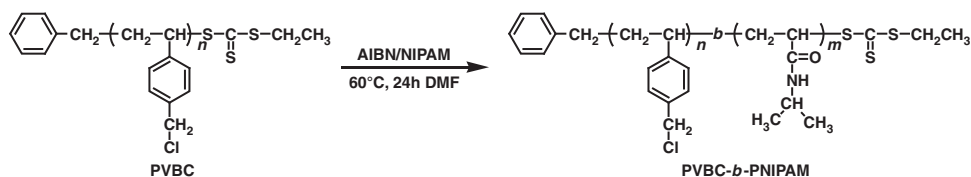
The ability to synthesize controlled architectures such as AB diblock copolymers is one of the features that distinguishes 'pseudo-living' from conventional free radical polymerization. As we had established RAFT polymerization conditions for VBC, for example, a PVBC homopolymer was used as the macro-RAFT agent for the subsequent block polymerization of NIPAM. The resulting amphiphilic AB diblock copolymer, which consists of hydrophobic and hydrophilic chain segments, will be a strong candidate for polymeric micelles.

The diblock copolymer was synthesized by RAFT polymerization of NIPAM using the macromolecular RAFT agent (macro-RAFT agent) PVBC (Scheme 2). The results are summarized in Table 2. In each case, the conversion of NIPAM is high (78%), and the SEC traces of the obtained block copolymers PVBC-*b*-PNIPAM exhibited unimodality and low PDIs. A shift toward higher  $M_n$  in all the SEC traces is observed in Figure 3, demonstrating the efficient block copolymer formation.

The structure of the block copolymer PVBC-*b*-PNIPAM is also confirmed by FT-IR and  $^1\text{H}$  NMR spectroscopy. The characteristic peak of amide carbonyl was observed at 1648  $\text{cm}^{-1}$ . The  $^1\text{H}$  NMR spectrum of the block copolymer PVBC-*b*-PNIPAM (No. 1) is shown in Supplementary Figure 1. The peaks corresponding to PVBC (a, b, c, d) and PNIPAM (e, f, h, i) are clearly observed. The compositions of PNIPAM in the block copolymers were determined from the integration ratios of the chloromethyl protons of PVBC and the methine protons of PNIPAM and were similar to the feed ratios of PVBC and NIPAM. The  $M_n$  determined by  $^1\text{H}$  NMR are quite close to the theoretical values at specific conversion, suggesting strong control of NIPAM polymerization with the macro-RAFT agent, and block copolymers PVBC-*b*-PNIPAM with low PDIs can be obtained by changing the macro-RAFT agent/NIPAM ratios.



**Figure 2**  $M_n$  and  $M_w/M_n$  of the products obtained from reversible addition-fragmentation chain transfer polymerization of vinylbenzyl chloride (VBC) with benzyl ethyl trithiocarbonate (BET) as a function of the conversion.  $[\text{AIBN}]_0$ : $[\text{BET}]_0$ : $[\text{VBC}]_0 = 0.25$ :1:100 at 70 °C under bulk conditions. AIBN, azobis(isobutyronitrile); NMR, nuclear magnetic resonance; SEC, size-exclusion chromatography.



**Scheme 2** Reversible addition-fragmentation chain transfer (RAFT) polymerization of *N*-isopropylacrylamide (NIPAM) with poly(vinylbenzyl chloride) (PVBC) as a macro-RAFT agent. AIBN, azobis(isobutyronitrile).

**Table 2** RAFT polymerization of NIPAM with a macro-RAFT agent (PVBC)<sup>a</sup>

No.	Feed.Ratio [AIBN] <sub>0</sub> : [PVBC] <sub>0</sub> : [NIPAM] <sub>0</sub>	Conv <sup>b</sup> (%)	Theo. <sup>e</sup>	M <sub>n</sub>			Composition <sup>d</sup> VBC:NIPAM(theo.)
				NMR <sup>f</sup>	SEC <sup>c</sup>	M <sub>w</sub> /M <sub>n</sub> <sup>c</sup>	
1	0.25:1:50	99.0	12 700	11 900	15 000	1.24	52:48 (50:50)
2	0.25:1:100	78.3	15 800	17 200	22 900	1.22	33:67 (37:63)
3	0.25:1:200	79.8	25 100	30 700	24 600	1.35	18:82 (22:78)

Abbreviations: AIBN, azobis(isobutyronitrile); DMF, dimethylformamide; NIPAM, *N*-isopropylacrylamide; NMR, nuclear magnetic resonance; PVBC, poly(vinylbenzyl chloride); RAFT, reversible addition-fragmentation chain transfer; SEC, size-exclusion chromatography; Theo., theoretical; VBC, vinylbenzyl chloride.

<sup>a</sup>Solvent: DMF (concentration: 1 mol/l to NIPAM).

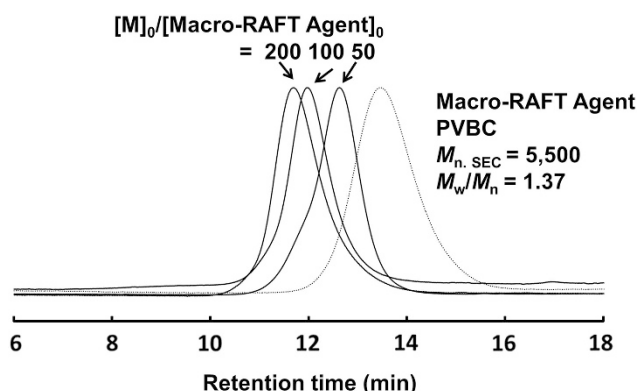
<sup>b</sup>Determined by <sup>1</sup>H-NMR analysis of the crude product.

<sup>c</sup>Determined by SEC based on polystyrene standards (eluent: DMF).

<sup>d</sup>Calculated by <sup>1</sup>H-NMR spectrum.

<sup>e</sup>The theoretical M<sub>n</sub> values were calculated on the basis of the conversion of NIPAM.

<sup>f</sup>The M<sub>n</sub> values were calculated by end-group analysis.



**Figure 3** Size-exclusion chromatography (SEC) traces of poly(vinylbenzyl chloride) (PVBC) macro-reversible addition-fragmentation chain transfer (RAFT) agent (dotted line, M<sub>n, NMR</sub> = 7000, M<sub>n, SEC</sub> = 5500, M<sub>w</sub>/M<sub>n</sub> = 1.37) and the products obtained from polymerization of *N*-isopropylacrylamide with a PVBC macro-RAFT agent.

## CONCLUSIONS

We demonstrated that PVBC with controlled molecular weight and polydispersity was obtained by RAFT polymerization of VBC, using BET as the chain transfer agent. Furthermore, amphiphilic AB diblock copolymers could be successfully prepared by RAFT polymerization of NIPAM using the macro-RAFT agent PVBC. PVBC with controlled molecular weight and polydispersity as well as their block copolymers will likely be used as the intermediates for the synthesis of various functional polymers.

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