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Synthesis of Bimodal Methacrylic Acid Oligomers by Template Polymerization

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ABSTRACT: A multivinyl template monomer with 20.4 methacryloyl groups was synthesized with β-cyclodextrin by esterification of hydroxyl groups with methacrylic anhydride. Copper-mediated atom transfer radical polymerization of the template monomer was carried out with methyl 2-bromopropionate, 2,2′-dipyridyl, and CuBr as an initiator, a ligand, and a catalyst, respectively. The effects of solvent and polymerization temperature on the degree of polymerization in the template monomer were investigated by kinetic analysis of conversion and the molecular weight of methacrylic acid oligomers obtained by hydrolysis of the polymerized products by GPC. Poly(methacrylate) oligomers with 7 and 14 degrees of polymerization were synthesized along the rims of the template monomer-3 by ATRP in a methanol/water mixture (water 10 vol %) at 50 °C. The observed propagation rate constant, k_{obs}, of the methacryloyl group in the methanol/water mixture (water 10 vol %) at 50 °C was 11.3×10^{-5}/s.

Introduction

Template polymerization is a useful technique for controlling the stereochemistry of polymerization.[1−7] When linear polymers are used as the templates, generally, the molecular weight and molecular weight distribution of daughter polymer can be controlled. However, the higher conversion of the polymer and unsuitable molecular weight of the template monomer lead to broad polydispersities.[8] For strict control of polymerization by template polymerization, the arrangement of vinyl groups in the template polymer and the strict control of radical concentration are required. β-Cyclodextrin is a stereochemically pure macrocyclic compound with 7 primary hydroxyl groups and 14 secondary hydroxyl groups. When the 14 secondary hydroxyl groups are modified with methacryloyl groups, a β-cyclodextrin template monomer with well-arranged vinyl groups is obtained. We have synthesized a β-cyclodextrin template monomer, in which 10.9 of the secondary hydroxyl groups are modified with vinyl groups and polymerized by free radical polymerization with α,α'-azobis(isobutyronitrile) (AIBN).[9] Because of the lack of the control of the initiation position and the radical concentration, the degree of polymerization, DP, of the vinyl groups in the template monomer was polydisperse.

Controlled/living radical polymerization is another approach for controlling radical concentration and polymerization rate.[10−19] By combining a controlled/living radical polymerization with a template polymerization, the polymerization was much controlled if the DP was low.[9,20] In contrast to AIBN, when the β-cyclodextrin template monomer was polymerized with *p*-xylyl *N*,*N*-dimethyldithiocarbamate (XDC)[9] and α-bromo-*p*-xylyl *N*,*N*-dimethyldithiocarbamate (BXDC) by the ATRP technique,[9] the DP of the vinyl group in the β-cyclodextrin template monomer, from 10 to 14, showed a good agreement with the number of vinyl groups in the β-cyclodextrin template monomer. However, XDC and BXDC were not adequate initiators for the β-cyclodextrin template monomer because XDC and BXDC were included in the β-cyclodextrin template monomer.[9]

On the other hand, atom-transfer radical polymerization, ATRP, is one of the most successful controlled/living radical polymerization techniques.[15,16,18,19] The polymerization temperature and solvent can be widely changed for ATRP. The β-cyclodextrin template monomer was polymerized with 1,3-dibromobutane/CuBr/1,1,4,7,10,10-hexamethyltriethylenetetramine by the ATRP technique.[20] By ATRP, the dispersity of the DP of the vinyl groups in the template monomer was decreased by decreasing not only the polymerization temperature but also the mobility of the vinyl groups in the template monomer. However, it was impossible to synthesize the completely monodispersed products because the number of vinyl groups in the template monomer was not monodispersed.

To strictly control the polymerization, the number of vinyl groups in the template monomer should be monodispersed. However, it was stereochemically difficult to synthesize the β-cyclodextrin template monomer with 7.0 and 14.0 acetyl and vinyl groups introduced into primary and secondary hydroxyl groups in a good yield. It was difficult to completely prevent the esterification of secondary hydroxyl group with acetic acid during the esterification of primary hydroxyl groups. On the other hand, Bowen and co-workers[21,22] reported the complete esterification of both primary and secondary hydroxyl groups in β-cyclodextrin with methacrylic anhydride for the synthesis of a novel cross-linker for dental materials. Seven and 14 vinyl groups were arranged on both sides of the β-cyclodextrin ring of the β-cyclodextrin template monomer with 21 vinyl groups. Again, luck of the distribution of number of vinyl groups in the template monomer is important to clarify the effect of the template structure on the template polymerization. If the molar ratio of the ATRP initiator to the template monomer with 21 vinyl groups is 2.0, the DP of vinyl group in the template monomer will be 7 and 14. In other words, methacrylic acid oligomers (PMAA) with DP = 7 and 14 will be obtained by hydrolysis of the

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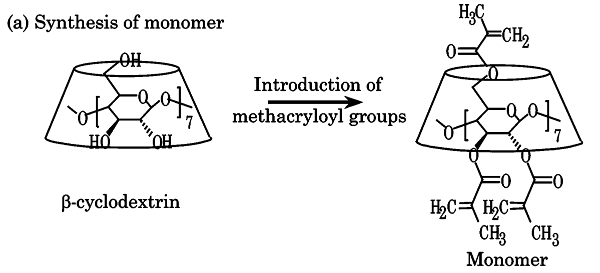
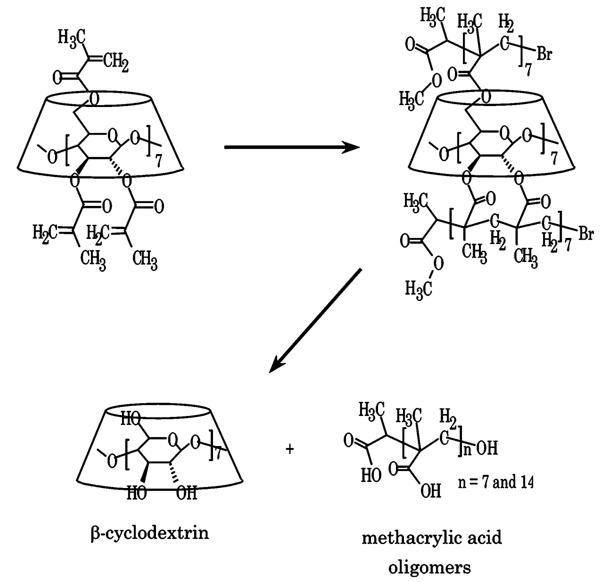
Scheme 1. Synthetic Concept of Copper-Based Atom Transfer Radical Polymerization of the β-Cyclodextrin Template Monomer

(a) Synthesis of monomer



(b) ATRP of template monomer



polymerized products. This concept of the template polymerization is shown in Scheme 1.

The purpose of this work is to investigate the structural effect of the β-cyclodextrin template monomer with 21 vinyl groups on the template polymerization by the ATRP technique. Methyl 2-bromopropionate, CuBr, and 2,2′-dipyridyl were chosen as an initiator, catalyst, and a ligand, respectively. The ATRP was carried out in methanol, a methanol/water mixture, and tetrahydrofuran (THF). The polymerization temperature was changed from 25 to 65 °C. The changes of conversion of vinyl group and the DP of PMAA were investigated by gel permeation chromatography (GPC).

Experimental Section

Materials. β-Cyclodextrin (Kanto Chemical Co., Inc.) was dried at 100 °C overnight under vacuum. Methacrylic anhydride (Aldrich, 94%), pyridine (Tokyo Chemical Industry Co., Ltd., 99.5%), hydroquinone (Kanto Chemical Co., Inc., 99%), methanol (Tokyo Chemical Industry Co., Ltd., 99.8%), toluene (Tokyo Chemical Industry Co., Ltd., 99.5%), copper(I) bromide (CuBr, Wako Pure Chemical Industries, Ltd., 99.9%), methyl 2-bromopropionate (Tokyo Chemical Industry Co., Ltd., 98%), and 2,2′-dipyridyl (bpy, Aldrich, 99%) were used without purification.

Synthesis of (2,3-Di-*O*-methacrylated-6-methacrylated)-β-cyclodextrin (Template Monomer). On the basis of ref 21, the vinyl groups were introduced into the hydroxyl groups of β-cyclodextrin in 13.6−54.7 wt % yields. The conditions are listed in Table 1. The typical procedure of template monomer is described as follows: β-Cyclodextrin (0.9 g, 0.792 mmol, 16.65 mmol of hydroxyl group) and hydroquinone (0.01 g 0.091 mmol) were dissolved in pyridine (18, 4.5, and 4.5 mL for the template monomer-1, -2, and -3, respectively). Methacrylic anhydride (4.96 mL, 33.3 mmol) was added to the solution. The solution was then refluxed at 50 °C for 5 h for template monomer-1 and -3 and for 3 h for template monomer-2. The product was precipitated into cold (5 °C) water (100 mL), purified by reprecipitation with methanol (10 mL) and water (50 mL), collected, and dried under vacuum. The number of vinyl groups introduced to β-cyclodextrin was characterized by ^{1}H NMR with *d*-chloroform. The average number of vinyl groups introduced to β-cyclodextrin determined was 20.4 for the template monomer-3. Yield: 39.4%. ^{1}H NMR (500 MHz, $CHCl_3$-d_6): δ [ppm] = 5.18 (7H, C(1)H of β-CD), 4.80 (7H, C(2)H of β-CD), 4.60 (7H, C(3)H of β-CD), 3.58 (7H, C(4)H of β-CD), 3.95−4.37 (7H, C(5)H and 14H, C(6)H of β-CD), 5.62 (20.8 H, $CH_2{=}C$ in methacryloyl), 6.17 (20 H, $CH_2{=}C$ of methacryloyl), 1.95 (61.2 H, CH_3 in methacryloyl).

Typical ATRP of the Template Monomer. The products were prepared by ATRP in 29.0−89.7 wt % yields. The ATRP conditions are listed in Table 2. The following is a typical procedure of ATRP. For MW-25-2, template monomer (1.0 g, 0.396 mmol, 80.78 mmol of vinyl group), toluene (0.2 mL, 1.98 mmol), methanol (100 mL), methyl 2-bromopropionate (0.091 mL, 0.792 mmol), bpy (0.309 g, 1.98 mmol), and CuBr (0.114 g, 0.792 mmol) were added to a sealable Pyrex reactor. The solution in the reactor was degassed using three freeze−pump−thaw cycles. The reactor was sealed under vacuum and heated at 25 °C for 4.0 h. To stop the polymerization, product was precipitated in water (200 mL), collected, and purified by reprecipitation for two times from methanol (10 mL) into cold (0 °C) water (50 mL). The product was white powder. Yield: 59.9 wt % for MW-25-2.

When the methanol was used as a solvent, the solution was evaporated under vacuum after the polymerization. Then, the product was purified and dried as well as above. Conversion of reacted vinyl group was determined by GPC with double detected equipment (RI and UV at 292 nm).

Hydrolysis of the Polymerized Products.[20] Polymerized product (0.1 g, 0.037 mmol) was dissolved in methanol (4.0 mL). Sodium hydroxide (0.04 g, 1.0 mmol) was added to the solution. The solution was stirred at room temperature for 4 h. The solution was poured to acetone (20 mL). Product was washed with 0.1 N HNO_3 (20 mL), collected, and dried. The degree of hydrolysis in the product was determined by ^{1}H NMR spectroscopy. Yield: 60 wt %.

^{1}H NMR (methanol-d_4): δ [ppm] = 0.8−1.2 (3H, CH_3), 1.9−2.0 (2.2H, CH_2).

Molecular Weight Measurements. Number-average molecular weight (M_n) and distribution of molecular weight (M_w/M_n) of the polymerized products and methacrylic acid oligomers (PMAA) were measured with gel permeation chromatography (Tosoh, GPC-2010) double detected with refractive index and ultraviolet at 292 nm. The column was a TSK-α-2500 (the range of M_w: 200−5 × 10^3). Eluent, flow rate, and temperature were THF, 0.6 mL/min, and 35 °C for polymerized products and methanol, 0.6 mL/min, and 30 °C for PMAA. The calibration curves[20] of PMAA previously prepared by combining GPC and matrix-assisted laser desorption ionization time-of-flight (MALDI−TOF) mass spectrometry were used.

Molecular weights of template monomer-3, polymerized product, and hydrolyzed product were measured with matrix-assisted laser desorption ionization time-of-flight (MALDI−TOF) mass spectrometry (Shimazu, Kraros Kompact MALDI 2) incorporating a 337 nm nitrogen laser with a 5 ns pulse duration (30 μm spot size). The instrument was operated at positive state in a linear mode with an accelerating potential of 20 kV. The accumulation number of laser shot was 100. For a matrix solution, 2,5-dihydroxybenzoic acid (300 mg, 1.77 mmol) was dissolved in acetone (3 mL), and then sodium trifluoroacetate (3 mg, 0.022 mmol) was added to the solution. β-Cyclodextrin solution was prepared by dissolving β-cyclodextrin (2 mg, 0.0018 mmol) in a methanol/water mixture (1 mL of methanol and 1 mL of water). Template monomer-3 solution was prepared by dissolving template monomer-3 (30

Table 1. Conditions and Results of Synthesis of Multimonomer with β-Cyclodextrin[a]

sample code	concn of β-cyclodextrin (mM)	concn of hydroxyl group (M)	reaction time (h)	yield (wt %)	av no. of methacryloyl groups in template monomer[b]
monomer-1	19.8	0.883	5.0	54.7	9.33
monomer-2	79.2	3.61	3.0	13.6	15.47
monomer-3	79.2	3.66	5.0	39.4	20.4

[a] Molar ratio of methacrylic anhydride to hydroxyl group: 2.0. Hydroquinone: 9.08 mM. [b] Determined by ^{1}H NMR.

Table 2. Conditions and Results of ATRP for Template Monomer-3 with Methyl 2-Bromopropionate as an Initiator

sample code[a]	concentration (mM)					temp (°C)	reaction time (h)	yield (wt %)	conv of vinyl group (mol %)[b)]
	multimonomer	initiator	ligand	CuBr	toluene				
MW-25-1	3.96	7.92	19.81	7.92	0.00	25	4	89.7	6.9
MW-25-2	3.96	7.92	19.81	7.92	19.81	25	4	59.9	25.3
MW-25-3	3.96	7.92	19.81	7.92	19.81	25	8	52.1	22.8
MW-25-4	7.92	15.85	39.60	15.85	39.60	25	4	gel	
MW-25-5	3.69	39.6	19.81	7.92	19.81	25	4	88.2	44.1
MW-25-6	3.96	7.92	99.05	7.92	19.81	25	4	70.9	26.3
MW-35-1	3.96	7.92	19.81	7.92	19.81	35	4	55.2	35.8
MW-50-1	3.96	7.92	19.81	7.92	19.81	50	4	82.5	36.1
MW-65-1	3.96	7.92	19.81	7.92	19.81	65	4	gel	
M-25-1	3.96	7.92	19.81	7.92	19.81	25	4	49.0	4.8
TW-25-1	3.96	7.92	19.81	7.92	19.81	25	4	57.8	9.1

[a] MW, M, and TW in the sample code indicate a methanol/water mixture (water 10 vol %), methanol, and a tetrahydrofuran/water mixture (water 10 vol %), respectively; middle numbers in the sample code indicate polymerization temperature. [b] Determined by UV absorption in methanol at 292 nm.

μg,) in methanol (30 μL) and adding 70 μL of the matrix solution and β-cyclodextrin solution to the template monomer-3/methanol mixture. PMAA solution was prepared by dissolving the hydrolyzed product (30 μg) in methanol (300 μL) and adding the matrix solution (70 μL) and β-cyclodextrin solution (10 μL). Then, the solution was loaded onto a stainless steel sample plate (about 100 μm spot size of simple), and the solvent was evaporated.

^{1}H NMR Measurement. ^{1}H NMR measurement was carried out with a ^{1}H NMR spectrometer (JEOL, GSX-500 Hz) with deuterated chloroform ($CHCl_3$-*d*) as a solvent at room temperature using the signal of the deuterated solvent as lock and the internal standard for chemical shift data in the δ-scale relative to TMS.

X-ray Fluorescence (XRF) Analysis. Chemical analyses were carried out in MW-50-1 by X-ray fluorescence (Philips PW2404 sequential spectrometer) fitted with a rhodium target end window and Philips UniQuant4 analytical software.

Results and Discussion

Synthesis of the Template Monomer. First, template monomer-1 was synthesized by esterification of hydroxyl groups of β-cyclodextrin with methacrylic anhydride. Table 1 presents the conditions of template monomer synthesis. The modification of hydroxyl groups with methacrylate was investigated by FT-IR measurement. Figure 1 shows the FT-IR spectra of β-cyclodextrin and the template monomer-3. After modification, the peaks at 3381 and 1158 cm^{-1}, owing to hydroxyl group, were decreased, and new peaks at 1723, 1637, and 814 cm^{-1} assigned to carbonyl, vinyl, and methyl groups, respectively, appeared. This indicates that the methacrylate was formed.

Then, the number of vinyl groups in the template monomer was determined by ^{1}H NMR. Figure 2a shows the ^{1}H NMR spectra of the template monomer-3. The signals of methylene proton of vinyl group, the methyl protons of methacrylate, and the protons of β-cyclodextrin scaffold were observed. The number of vinyl groups in the template monomer-3 calculated by using the peaks of C(7)H of vinyl group and C(1)H peak of β-cyclodextrin observed at 5.62−6.17 and 5.18, respectively, was 20.4. Additionally, the ratio of the area of C(7)H peaks of the vinyl group and the total area of protons of β-cyclodextrin scaffold, C(1)H−C(6)H, was 0.83. The average number of vinyl groups in the themplate monomer calculated from the ratio of areas of C(7)H peaks and proton of β-cyclodextrin, 20.3, agreed well with the average number of vinyl group calculated with the peaks of C(7)H and C(1). The numbers of vinyl group in the template monomers calculated with the peaks of C(7)H and C(1) are listed in Table 1. The average number of vinyl groups in the template monomer was increased by increasing the concentration of β-cyclodextrin and reaction time. However, it was impossible to perfectly obtain the template monomer with 21 vinyl groups.

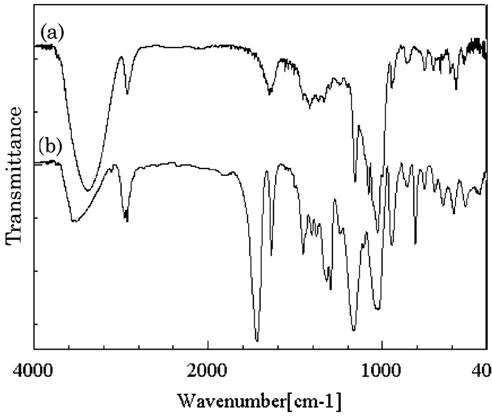


Figure 1. FT-IR spectra of β-cyclodextrin (a) and the template monomer-3 (b).

The template monomer-3 with 20.4 vinyl group would be a mixture of the template monomer with 21 vinyl groups and the template monomer with less than 20 vinyl groups. The formation of the template monomer with 21 vinyl groups was confirmed By MALDI−TOF mass measurements. Figure 3a shows the MALDI−TOF mass spectra of the template monomer-3. The peak numbers in Figure 3a indicate the number of vinyl groups and the structure of ion. For example, peak 19b corresponds to template monomer with 19 vinyl groups with the structure b, i.e., [M + H]$^+$. All structures of ions and the observed and calculated mass values are

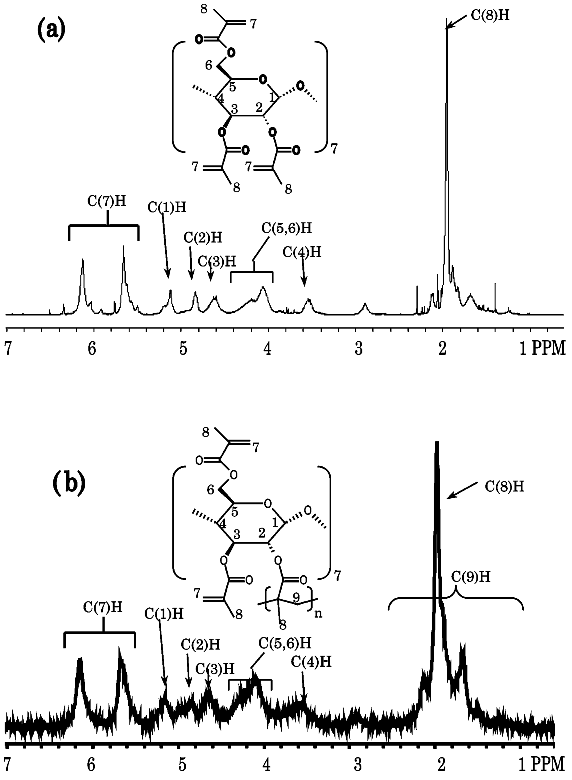


Figure 2. ^{1}H NMR spectra of the template monomer-3 (a) and MW-50-1 (b).

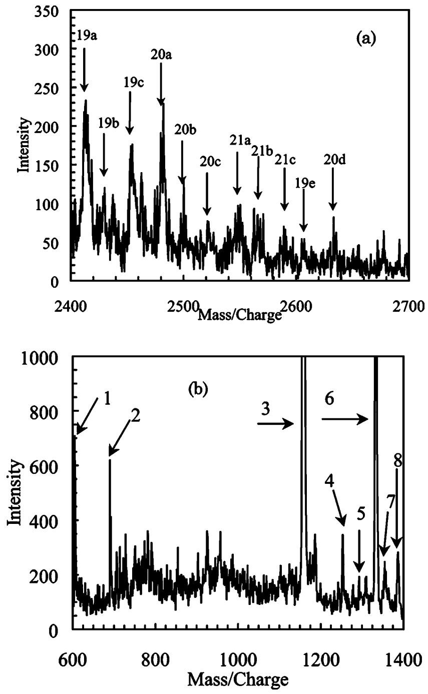


Figure 3. MALDI−TOF mass spectra of the template monomer-3 (a) and PMAA obtained from MW-50-1 (b).

Table 3. MALDI−TOF Mass Peaks of Template Monomer-3

structure[a]	peak type[b]	no. of vinyl groups 19	20	21
$[M + H - H_2O]^+$	a observed	2412	2479.9	2548.3
	a calculated	2411.71	2479.8	2547.89
$[M + H]^+$	b observed	2430	2497.7	2565.9
	b calculated	2429.71	2497.8	2565.89
$[M + Na]^+$	c observed	2452	2521.3	2589
	c calculated	2451.7	2519.79	2587.88
$[M + H - H_2O]^+ +$ DHBA	d observed		2633.2	
	d calculated	2565.71	2633.8	2701.89
$[M + Na]^+ +$ DHBA	e observed	2604.9		
	e calculated	2605.7	2673.79	2741.88

[a] M and DMBA correspond to template monomer molecule and 2,5-dihydroxybenzoic acid included in template monomer molecule, respectively. [b] Peak types a−e correspond to the peak types shown in Figure 3a.

listed in Table 3. Three peaks of the template monomer with 21 vinyl groups with different ion structures were clearly observed at 2548.3, 2565.9, and 2598 for $[M + H - H_2O]^+$, $[M + H]^+$, and $[M + Na]^+$ ions, respectively. Taking account of the number of C, O, and H atoms of the template monomer-3 and isotopic abundance of these atoms, the ratios of peak intensity of isotopic molecular ion with +1, +2, and +3 to principal molecular ion of template monomer-3 are calculated in ranges of 1.31−1.4, 0.97−1.09, and 0.177−0.198 for 19, 20, and 21 vinyl groups. The side peaks of Figure 3a are the isotopic molecular ion peaks. Thus, the formation of the template monomer with 21 vinyl groups in the template monomer-3 was confirmed. However, the peaks owing to the template monomer with 19 and 20 vinyl groups were also observed. The peaks owing to the template monomer with 19 and 20 vinyl groups including DHBA, which is a matrix, were also observed at 2604.9 and 2633.2, respectively. The template monomer-3 was a mixture of the products with 19−21 vinyl groups. Taking account of the average number of the vinyl groups in the template monomer-3, the minimum molar fraction of product with 21 vinyl groups in the template monomer-3 was 0.4. The template monomer-3 was adequate for the template polymerization of this study.

ATRP of the Template Monomer-3. Template polymerization of the template monomer-3 by ATRP was carried out with methyl 2-bromopropionate, CuBr, and 2,2′-bipyridyl (bpy) as an initiator, catalyst, and ligand, respectively. Polymerization conditions and results are presented in Table 2. MW, M, and TW in the sample code indicate a methanol/water mixture with 10% of water, methanol, and a THF/water mixture with 10% of water, respectively, which were used as solvents. The second number in the sample code indicates reaction temperature. After ATRP, the gelation of systems did not seem to be observed. First, the MALDI−TOF mass measurements of the polymerized products were carried out. No peak was observed by MALDI−TOF mass measurements. Matrix and measurement conditions would be inadequate for the measurements.

For detailed investigation of the polymerization, GPC measurements were carried out for the polymerized products. Figure 4 shows the GPC profiles of the template monomer-3 and the polymerized products. A single peak was observed for the template monomer-3. After ATRP, the shape and position of the peaks of polymerized products, except for MW-25-4 and MW-65-1, well agreed with those of the template monomer-3. This indicates that the ATRP was limited in the template monomer molecule when the monomer concentration was 3.96 mM and reaction temperature was less than 50 °C. New broad peaks appeared at higher molecular weight for MW-25-4 and MW-65-1, indicating the polymerization between the molecules. Consequently, the polymerization of the template monomer-3 was successfully limited in the molecule of template monomer when the template monomer concentration and the concen-

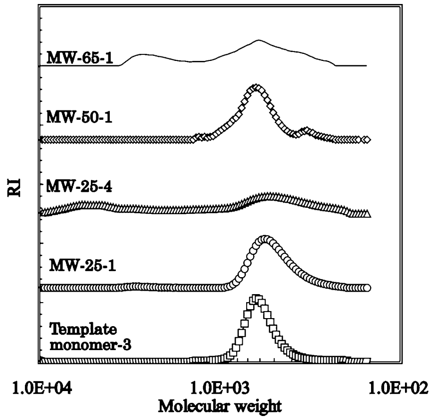


Figure 4. GPC profiles of the template monomer and the products polymerized in a methanol/water mixture (water 10 vol %) with [monomer-3]:[initiator]:[CuBr]:[bpy]:[toluene] = 1:2:2:5:5. MW-25-2: at 25 °C at [monomer-3] = 3.96 mM. MW-25-4: at 25 °C at [monomer-3] = 7.92 mM. MW-50-1: at 50 °C at [monomer-3] = 3.96 mM. MW-65-1: at 65 °C at [monomer-3] = 3.96 mM.

tration of vinyl group were 3.96 mM and 80.78 mM, respectively, under 50 °C. Here, it should be noticed that the concentration of vinyl groups in the solution of this work was higher than that of the previous works with the template monomer with 10.6 of vinyl groups (the concentration of template monomer: 4.12 mM; concentration of vinyl group: 43.7 mM).[9,20] Although the concentration of the vinyl groups of this work was much higher than the previous works,[9,20] the macrogelation of the systems was successfully hindered. It would be due to the template effect of β-cyclodextrin.

The conversion of the vinyl groups in the template polymer was investigated by ^{1}H NMR measurements. Figure 2b shows ^{1}H NMR spectra of MW-25-3. The signals of vinyl protons observed at 5.8 and 6.0 ppm were decreased, and a new broad peak owing to the methine and methylene protons in the backbone of polymerized methacrylate appeared. Therefore, the polymerization of vinyl groups in the template monomer-3 was confirmed. However, the signal of methyl proton of the initiator was not observed due to the screening by the signals owing to the β-cyclodextrin ring. From the peak areas of peaks a and b, the conversion of the vinyl group of MW-25-3 was 21.1 mol %. The conversion of the vinyl group of MW-25-3 calculated from the areas of GPC peaks detected by RI and UV at 292 nm, 22.8 mol %, showed a good agreement with that by the ^{1}H NMR method. The conversions of ATRP products determined by GPC with RI and UV detection are presented in Table 2.

Addition of toluene, which is an inclusion compound, to β-cyclodextrin and the increase of temperature and time of polymerization raised the conversion of the vinyl group. For example, the conversion of the vinyl group with toluene was drastically increased to 25.3 mol % of MW-25-2 from 6.9 mol % of MW-25-1. Previously, we found that the inclusion of toluene to the template monomer with 10.6 vinyl groups improved the conversion due to the prevention of the inclusion of vinyl groups into the β-cyclodextrin ring of the template monomer.[19] As well as previous work,[19] the inclusion of vinyl groups into the cavity of the β-cyclodextrin ring of the template monomer-3 would be prevented by addition of toluene; thereby, the conversion of the vinyl group would be increased.

Then, a solvent effect on the conversion was investigated. MW-25-2, M-25-1, and TW-25-1 were polymerized in a methanol/water mixture, methanol, and a THF/water mixture, respectively. In this work, THF was not used as a solvent because it was difficult to dissolve CuBr in THF. The reaction temperature and the molar ratio of the initiator to the template monomer-3 of MW-25-2, M-25-1, and TW-25-1 were 25 °C and 2.0, respectively. For copper-mediated ATRP, solvent polarity has a positive effect on the activation rate parameters of butyl acrylate radical.[23] Additionally, the addition of a polar solvent to the system increases the solubility of Cu(I) and Cu(II) species, thereby increasing the concentration of deactivator in the reaction solution.[24] Thus, from the viewpoint of the reactivity of the living radical of the methacrylate, the increasing of the conversion was expected by adding water to the system. As expected, the conversion of the vinyl group of MW-25-2 polymerized in the methanol/water mixture was drastically higher than those of M-25-1 and TW-25-1 polymerized in methanol and the THF/water mixture, respectively. Consequently, the methanol/water mixture with 10% of water was an optimum solvent for the ATRP for the template monomer-3.

Finally, the effects of molar ratios of the initiator and the ligand to the template monomer on the conversion were investigated. The conversion of MW-25-5 with 5.0 of the molar ratio of an initiator to the template monomer-3, 44.1 mol %, was clearly improved from that of MW-25-2, 25.3 mol %. On the other hand, the conversion of vinyl groups was not improved by increasing the molar ratio of ligand to the template monomer-3 (see MW-25-2 and MW-25-6). Thus, it was found that the increase of the molar ratio of an initiator to the template monomer-3 was effective to increase the conversion of vinyl groups. The effect of molar ratio of an initiator to the template monomer-3 on the degree of polymerization of methacrylates is discussed in a later section.

To investigate the progress of ATRP in the template monomer-3, the methacrylic acid oligomers (PMAA) were detached from the polymerized products by hydrolysis. Figure 3b shows MALDI−TOF mass spectra of PMAA synthesized from MW-50-1. Peaks 1 and 2 were observed at 606.6 and 692.5, respectively, owing to $[\text{PMAA} + \text{H}]^+$ with DP = 6 and 7, whose theoretical principal molecular weights were 606.3 and 692.3, respectively. From 700 to 1165, clear peaks were not detected. Peaks 3 and 6 at 1165.5 and 1333.9, respectively, were β-cyclodextrin and β-cyclodextrin with 2,5-dihydroxybenzoic acid and 2 Na, respectively. Peak 4 observed at 1254 was owing to $[\text{PMAA} + \text{Na}]^+$ with Na and DP = 13, the theoretical principal molecular weight being 1252.5. The absence of peaks from 700 to 1200, except for the cyclodextrin peak, indicates that PMAA with DP = 7−12 did not exist in MW-50-1. The mass/charge values of peaks 5 and 8, 1293.2 and 1384.5, respectively, were assigned to $[\text{PMAA}]^+$ with DP = 14 with 0 and 4 Na, with the theoretical principal molecular weight 1293.6 and 1382.5, respectively. The mass/charge of peak 7, 1355.5, showed a good agreement with the theoretical principal molecular weight of $[\text{PMAA} + \text{H}]^+$ with 14 containing one Br group. Thus, the synthesis of PMAA with DP = 6, 7, 13, and 14 in MW-50-1 was confirmed.

It is difficult to quantitatively determine a content in a mixture of PMAA by MALD-TOF mass measure-

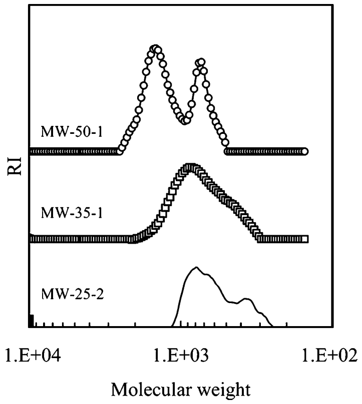


Figure 5. GPC profiles of methacylic acid oligomers obtained by hydrolysis of products polymerized in a methanol/water mixture (water 10 vol %) for 4 h with [monomer-3] = 3.96 mM, [initiator] = [CuBr] = 7.92 mM, and [bpy] = [toluene] = 19.81 mM. MW-25-2: 25 °C. For MW-35-1: 35 °C. MW-50-1: 50 °C.

ments. Thus, the GPC measurements were carried out. Figure 5 shows the GPC profiles of the PMAA measured with methanol. Each peak area corresponds to the conversion of the vinyl group. It should be noticed that the polymerization between the molecules of the template monomer-3 did not occur for all polymerized products shown in Figure 5. As expected from the MALDI−TOF mass spectra, the molecular weight distribution of PMAA of all products measured by GPC was bimodal. By comparison with the MALDI−TOF mass spectra observed in the previous work,[20] the molecular weight of PMAA of GPC profiles was calibrated. For MW-50-1, two clear peaks were observed at 700 and 1400 of the molecular weight, M_{PMAA}. These values well agreed with the M_{PMAA} values in cases of DP = 7 and 14, 705 and 1307, respectively. This indicates that the polymerization proceeded along both of the rims of the template monomer-3. Then, the peak areas of PMAA with different M_{PMAA} were compared. For MW-50-1, the ratio of peak area at $M_{\mathrm{PMAA}} = 1300$ to that at $M_{\mathrm{PMAA}} = 700$ was 1.83. If the ATRP was randomly initiated in both rims of the template monomer-3, the molar ratio of PMAA with $M_{\mathrm{PMAA}} = 1300$ to that at $M_{\mathrm{PMAA}} = 700$ should be 1.0. In such a case, taking account of the molecular weight of PMAA, the ratio of peak area at $M_{\mathrm{PMAA}} = 1300$ (DP = 14) to that at $M_{\mathrm{PMAA}} = 700$ (DP = 7) is 2.0. The experimental value, 1.83, is close to the theoretical value. Consequently, the polymerization was completed on both rims in the template monomer-3 at 50 °C.

Although the GPC results suggested that the polymerization was completed on both side of the rims, the conversion of vinyl groups of MW-50-1 was 36.1%. To investigate this point, the introduced amount of initiator to the template monomer-3 was estimated by the measurement of the Br group concentration in MW-50-1. XRF analysis confirmed that the amount of Br in MW-50-1 was 5.30 wt %. Taking account of the conversion of vinyl group of MW-50-1, 36.1 mol %, the average DP to a Br group was 10.36. On the other hand, the theoretical average DP for the mixture of PMAA with DP = 7 and 14 is 10.5. The experimental and theoretical average DP values agreed well. Thus, the low conversion of the polymerization suggests that not all of the initiator was introduced in the template monomer-3; however, the ATRP, which was started with the initiator introduced into the template monomer-3, was completed on both rims.

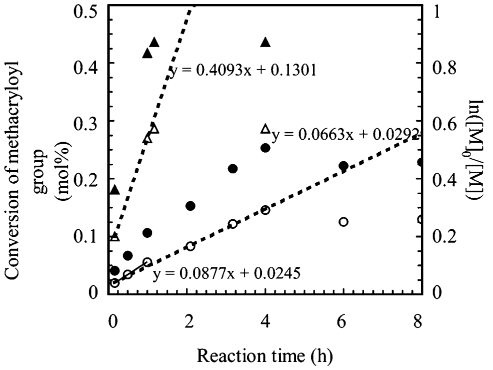


Figure 6. Kinetic plots for the ATRP of methacryloyl group in a methanol/water mixture (water 10 vol %). [Monomer-3] = 3.96 mM, [initiator] = [CuBr] = 7.92 mM, [bpy] = [toluene] = 19.81 mM. Closed circle: conversion at 25 °C. Open circle: $-\ln[M]_0/[M]$ at 25 °C. Closed triangle: conversion at 50 °C. Open triangle: $-\ln[M]_0/[M]$ at 50 °C.

At 25 °C, the M_{PMAA} decreased and the M_{PMAA} peaks were broadened. The lower polymerization temperature generally decreases the polymerization rate. Because of the slower initiation rate than the polymerization rate, the distribution of molecular weight is relatively wide in the early stage of polymerization. As discussed in latter section, however, the conversion of vinyl group of MW-25-2 was saturated at 4 h. In other words, the polymerization of MW-25-2 was completed at 4 h. This suggests that the lower M_{PMAA} values and the broader M_{PMAA} peaks of MW-25-2 would not be due to the incomplete of polymerization. For clarification of this point, further investigation is required. However, the further investigation about this point was not carried out in this work.

Kinetic Analysis of the ATRP for the *β*-Cyclodextrin Template Monomer. Next, ATRP of vinyl groups in the template monomer-3 was investigated from a kinetic viewpoint. Figure 6 shows the conversion curves of the vinyl group and kinetic points of MW-25-2 and MW-50-1. The saturation of the conversions of vinyl group at 4.0 and 1.0 h for MW-25-2 and MW-50-1 at 25 and 50 °C, respectively, indicates the complete polymerization. As described above, for MW-50-1, all of the vinyl groups in the rims, where the initiator was introduced, was completely polymerized at 4.0 h. The kinetic plots of MW-50-1 showed good linearity before the saturation. It is concluded that the polymerization of vinyl groups proceeded along the rims in the living manner at 50 °C. The observed polymerization rate, k_{obs}, of MW-50-1 was $11.3 \times 10^{-5}\ \mathrm{s}^{-1}$. Theoretically, two k_{obs} values should be observed for the kinetic plot of MW-50-1. However, because of the long interval of sampling time to compare to the polymerization rate, the change of k_{obs} was not observed for MW-50-1. The k_{obs} values of methyl methacrylate with CuBr and bpy at 80 °C were 3.52×10^{-5}[25] and $13.98 \times 10^{-5}\ \mathrm{s}^{-1}$[26] in bulk with 1-phenylethyl bromide and in ethyl acetate with ethyl 2-bromopropionate, respectively. The k_{obs} value of MW-50-1 was in the range of the reference values. Taking account of the polymerization temperature, the k_{obs} value of MW-50-1 was larger than the k_{obs} values without the template. Consequently, it was concluded that the polymerization was enhanced by the template.

In contrast to MW-50-1, the slope of the kinetic plot of MW-25-2 was changed at 1 h. In each region, the ATRP proceeded in a living manner since the kinetic

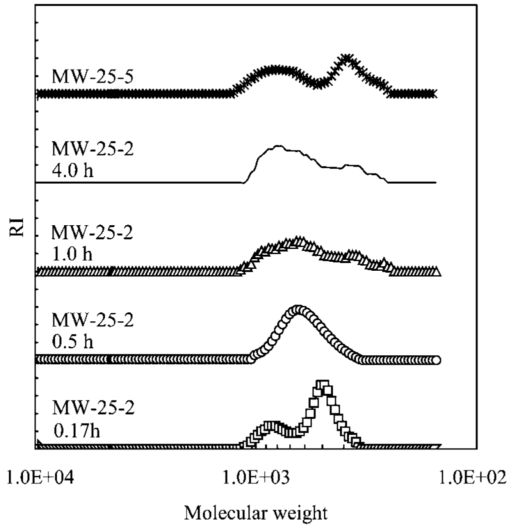


Figure 7. GPC profiles of methacrylic acid oligomers obtained by hydrolysis of MW-25-2 and MW-25-5 polymerized in a methanol/water mixture (water 10 vol %) at 25 °C. [Monomer-3] = 3.96 mM, [CuBr] = 7.92 mM, [bpy] = [toluene] = 19.81 mM. [Initiator] = 7.92 and 39.6 mM for MW-25-2 and MW-25-5, respectively.

plots of MW-25-2 show good linearity. The k_{obs} values of MW-25-2 were 2.43×10^{-5} and 1.75×10^{-5} s^{-1}until 1 h and from 1.0 to 4.0 h, respectively. The change of the slope suggests the complete of the polymerization of the vinyl groups on the rim having seven vinyl groups.

However, the saturated conversion of the vinyl group of MW-25-2 at 4.0 h was clearly lower than that of MW-50-1. To investigate the proceeding of the polymerization and the M_{PMAA}, the GPC measurements of PMAA of MW-25-2 and MW-25-5 were carried out.

Figure 7 shows the GPC profiles of PMAA of MW-25-2 at different reaction time and MW-25-5 at 4 h. Because of fast polymerization of MW-50-1, the time dependence of M_{PMAA} of MW-50-1 could not be observed. The single GPC peak should be shifted to higher molecular weight by increasing the reaction time in the early stage of the polymerization. However, the peak was bimodal at 0.17 h. From the peak area, the major product at 0.17 h was PMAA with $M_{PMAA} = 500$. The peak at 0.5 h was unimodal but broad. Then, the peak became bimodal again. The major product at 4.0 h was PMAA with $M_{PMAA} = 800$. Theoretically, the M_{PMAA} product in the early stage, at 0.17 h, should not be unity. However, the maximum DP of this work is too small to neglect the inhomogeneity of the initiation. To compare with the conventional radical polymerization, the concentrations of the initiator and the template monomer-3 of this work were low. Thus, the initiation time of the polymerization might be relatively longer than that of the conventional radical polymerization. As a result, the inhomogeneity of initiation of ATRP caused the wider distribution of M_{PMAA} in this work. By proceeding the polymerization, the peak became single and broadened. The broadening of the peak at 0.5 h would be due to the shift of the major peak from lower molecular weight to the higher. Taking account of the shapes of peaks at 0.17 and 4.0 h, the unimodal peak at 0.5 h was composed with bimodal products with similar weight. It is concluded that two types of PMAA were synthesized in the template monomer-3 in any stage. After 1.0 h, the polymerization on the rim with 14 vinyl groups continued, and it was completed on the rim with 7 vinyl groups. Thus, the two k_{obs} values were observed for MW-25-2.

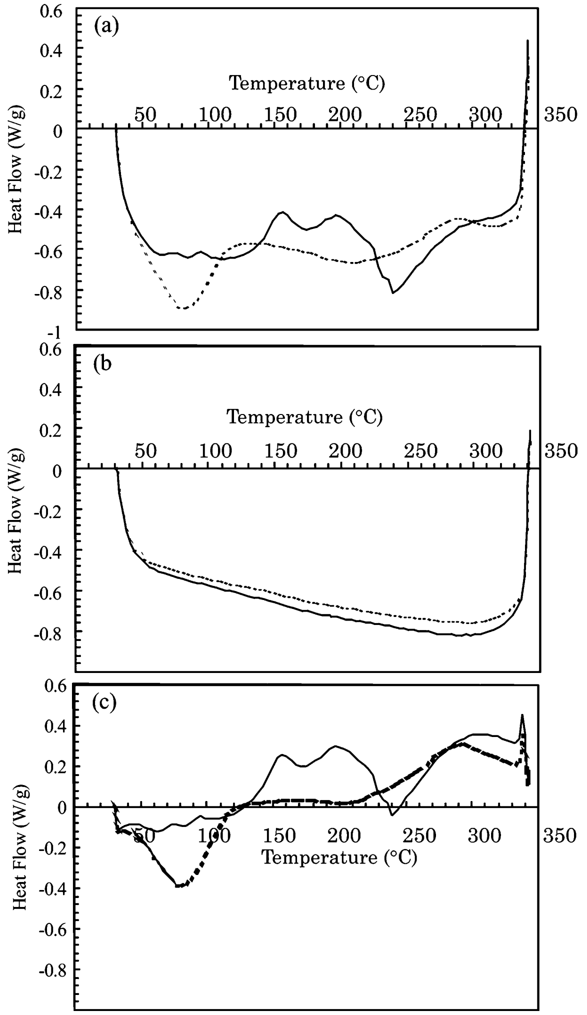


Figure 8. DSC profiles of the template monomer-3 (solid line) and MW-50-1 (dash line): (a) first scan, (b) second scan, (c) (a) − (b).

It should be noticed that the M_{PMAA} values of MW-25-2 at 4 h, 800 and 400, were much lower than those of MW-50-1. As described above, increasing of the initiator concentration at 25 °C enhanced the conversion of the vinyl groups. For MW-25-5, new PMAA with lower M_{PMAA} than MW-25-2 was additionally obtained. These indicate that the vinyl groups remained in the MW-25-2 were reactive with the radical provided with the initiator. However, the polymerization was not improved by increasing the initiator concentration. Therefore, the suitable polymerization temperature for the template polymerization of this work was 50 °C; it was impossible to control the template polymerization when the polymerization temperature was lower than 50 °C.

Finally, to investigate thermal properties of the template polymer-3 and MW-50-1, the DSC and TGA measurements were carried out. Figure 8 shows the DSC profiles of the template monomer-3 and MW-50-1. The template monomer-3 and MW-50-1 was mainly decomposed over 360 °C. Thus, the maximum temperature of DSC was set to be 350 °C. Taking account of the heat capacity of the compound, the first scanning data (Figure 8a) were corrected with the second scanning data (Figure 8b). Figure 8c were the corrected data

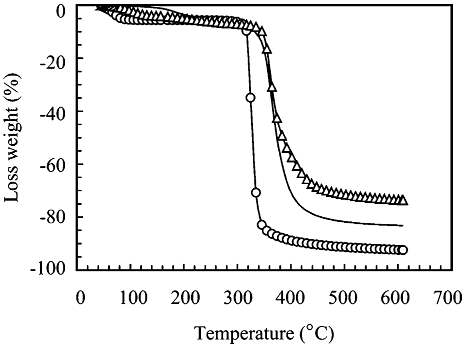


Figure 9. TGA profiles of β-cyclodextrin (circle), the template monomer-3 (triangle), and MW-50-1 (solid line).

of DSC. For the template monomer-3, two exothermic peaks owing to the vinyl groups were observed at 120−220 and 250−350 °C. It was found that there were type types of vinyl groups in the template monomer-3. The reactivity of the vinyl groups observed at 120−220 °C was higher than that at 250−350 °C. For MW-50-1, the exothermic peak at 120−220 °C vanished; an exothermic peak observed at 250−350 was still observed. This indicates that in MW-50-1 the vinyl groups with higher reactivity disappeared by ATRP; the vinyl groups with lower reactivity remained. The conversion of the vinyl group of MW-50-1 calculated from the DSC data, 52 mol %, did not agree with that determined by UV. To avoid the thermal degradation of the template monomer-3 and MW-50-1, the DSC measurements was stopped at 350 °C. Therefore, the conversions of the vinyl group measured by DSC and UV did not agree.

To investigate the thermal stability of the composites, TGA measurements were carried out under nitrogen. Figure 9 shows the TGA curves of β-cyclodextrin, the template monomer-3, and MW-50-1. The thermal decomposition temperatures of the template monomer-3 and MW-50-1 were drastically increased than that of β-cyclodextrin. Thus, thermal stability of the template monomer-3 and the polymerized products was improved by the modification of hydroxyl groups of β-cyclodextrin with methacrylates. The thermal degradation of PMMA synthesized by conventional radical polymerization has three degradation steps owing to the decomposition of the head-to-head linkage, vinylidene chain end, and unzipping of PMMA main chain in the ranges of 180−200, 240−320, and 320−440 °C, respectively.[27] However, for MW-50-1, the thermal degradation occurred at 180−200 and 320−440 °C, owing to the decomposition of head-to-head linkage and unzipping of main chain. It is reasonable that the decomposition at 240−320 °C is due to the decomposition from the vinylidene chain end. Methyl 2-bromopropionate was used as an initiator by the copper-mediated ATRP of MW-50-1; the chain end of the poly(methacrylate) was not the vinylidene group but the bromide group. The decomposition at 180−200 °C indicates that the linkages of vinyl groups in MW-50-1 were the mixture of head-to-head and head-to tail as well as conventional radical polymerization. In other words, it was impossible to stereochemically control the polymerization of vinyl groups even in the template monomer-3.

Conclusion

The β-cyclodextrin template monomer with 20.4 vinyl groups, the template monomoer-3, was synthesized by esterification of hydroxyl groups of β-cyclodextrin with methacrylic anhydride. ATRP of the template monomer-3 was carried out with methyl 2-bromopropionate, CuBr, and *N,N′*-dipyridyl as an initiator, a catalyst, and a ligand, respectively. The inclusion of toluene to the template monmer-3 and the increase of solvent polarity by adding small amount of water to the system were enhanced the conversion of vinyl groups. The conversion of the vinyl group showed the maximum at 3.90 mM of the template monomer-3 at 50 °C. ATRP over 3.90 mM of the template monomer-3 or over 60 °C caused the gelation of the systems. The molecular weight of methacrylic acid oligomers, PMAA, obtained by hydrolysis of the polymerized products was investigated by GPC. The PMAA mixture with 7 and 14 degrees of polymerization was synthesized at once by using the template polymerization of MW-50-1. The template monomer-3 was successfully polymerized by ATRP in a methanol/water mixture with 10 vol % at 3.90 mM of the template monomer concentration at 50 °C for 4.0 h (MW-50-1). For the case of MW-50-1, the copper-mediated ATRP for the template monomer-3 proceeded in a living manner with the observed polymerization rate, $11.3 \times 10^{-5}\ s^{-1}$, which was slightly larger than those for the conventional radical polymerization. At 25 °C, the molecular weight of the PMAA was increased by reaction time until 1.0 h. Thermal analysis by DSC and TGA indicated that the polymerization of vinyl group was not stereochemically controlled; in other words, the linkage of vinyl groups was the mixture of head-to-head and head-to-tail.

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