

ARTICLE

Synthesis and post-polymerization reaction of end-clickable stereoregular polymethacrylates via termination of stereospecific living anionic polymerization

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Poly(methyl methacrylate)s with high stereoregularity and clickable end-groups were synthesized via terminating reactions with α -(halomethyl)acrylates in stereospecific living anionic polymerization. The terminating reaction was so efficient and tolerant to the reaction conditions that almost quantitative end-functionalization was achieved in isotactic- and syndiotactic-specific polymerization systems. The terminating reactions were also achieved in the polymerizations of vinyl methacrylate and trimethylsilyl methacrylate. For the polymerization of butyl acrylate, however, the termination efficiency was limited as high as 69%. Further quantitative end-functionalization of the incorporated C=C double bond at ω -end was achieved with various thiols catalyzed by Et₃N. The base-catalysed thiol-ene reaction of the stereoregular poly(vinyl methacrylate) with ω -end C=C double bond proceeded selectively to retain vinyl ester functions, and the subsequent hydrolysis afforded ω -functional stereoregular poly(methacrylic acid). A combination of the terminating agent with a protected lithium amide afforded stereoregular poly(methyl methacrylates) with orthogonally clickable α - and ω -ends.

Introduction

End-functional polymers¹ have important roles not only in the synthesis of block copolymer² and branched copolymer³⁻⁵ but also in various application areas such as attachment of macromolecules onto material surfaces^{6,7} and construction of bio/artificial hybrid materials.⁸⁻¹⁰ In particular, since the facile and quantitative reaction systems based on the concept of 'click chemistry' have been established, polymers with clickable end-functionalities have attracted polymer chemists and material scientists.^{11,12} Clickable end-functionalities are generally introduced by living polymerizations with an initiator and/or a terminating agent bearing clickable functional groups or their precursors. For example, reversible addition fragmentation transfer (RAFT) polymerization gives a dithioester group in ω -end, which can be converted to thiol by a treatment with primary amine and then conducted to thiol-ene or thiol-yne click chemistry.¹²⁻¹⁵ Recently, Perrier *et al.* have reported a new chain transfer agent with carbonyl azide group, which affords the incorporation of an isocyanate group for click chemistry

into α -end.¹⁶ Another way from living polymerization to click chemistry is atom transfer radical polymerization (ATRP) and the following copper-catalyzed azide-alkyne cycloaddition (CuAAC) using azide group at ω -end derived from terminal halogen atoms. In fact, Matyjaszewski *et al.* have succeeded in the direct combination of ATRP and CuAAC reaction in one-pot system.¹⁷⁻¹⁹ Moreover, the conversions of bromo atom at ω -end to cyclopentadienyl group for Diels-Alder click reaction²⁰ and to thiol group for thiol-ene and thiol-yne click reaction²¹ are also possible. There are many reports on the ATRP initiators with clickable group, some of which are now commercially available.^{1,2,22,23}

Besides end-functionality, control of stereoregularity has also been a major target of precise polymerization chemistry,²⁴ because stereoregularity often affects polymer properties. For instance, isotactic poly(methyl methacrylate) (*it*-PMMA) have a glass transition temperature (T_g) around 50 °C, while syndiotactic (*st*-)PMMA exhibits T_g at 120 °C.²⁵ Therefore, numerous efforts have been paid for the control of stereoregularity of PMMA. In radical polymerization, highly

isotactic PMMAs (*mm* content > 99.9%) was synthesized via the polymerization of bulky monomers such as 1-phenylsuberyl methacrylate and the post-polymerization modification for isotactic polymer,²⁶⁻²⁸ and polymerization of MMA in fluoroalkyl alcohols for syndiotactic polymer (*rr* content = 93%).^{29,30} Furthermore, the simultaneous control of stereoregularity and molecular weight has been achieved by living radical polymerization at low temperature (~ -78 °C) in fluorine alcohols, where *st*-PMMA (*rr* content ~ 85%) could be synthesized.³¹ More sophisticated control of stereoregularity and molecular weight could be achieved by stereospecific anionic polymerizations, which afford stereoregular PMMAs with high tacticity (*mm* content ~ 99.5% for *it*-PMMA³² and *rr* content = 96% for *st*-PMMA³³) with narrow molecular weight distribution. In these stereospecific anionic polymerization systems, non-polar solvents such as toluene are used to facilitate interaction of the living polymer anion to counter cation or some additives, achieving the stereoregulation. As a consequence, the reactivities of the living anions are suppressed so low that they can scarcely react with typical terminating agents such as allyl³⁴ and benzyl³⁵ halides, generally used for anionic polymerization in polar solvents. Thus, multidentate or strong amine ligands are required to activate the living anions for the end-functionalization by terminating agents.³⁶ For a functional initiator approach, the reagent design should comply with the demand of proper reactivity to allow the simultaneous control of molecular weight and stereoregularity as well as of tolerance to their functional groups. In fact, there are only a few reports of functional initiator for stereospecific anionic polymerization of MMA.^{37,38}

Recently, we have found that α -(halomethyl)acrylates (**1**) are effective terminating agents for stereoregular PMMA living anions, where **1** undergoes addition-fragmentation reactions (S_N2' reaction) with nucleophiles (living PMMA anions) to give the polymers with ω -end functionality of α,β -unsaturated ester.³⁹ The resulting polymers are susceptible to further chemical modification via Michael addition click chemistry. In this article, we report the details and advanced results of the termination and the subsequent end-functionalization.

Experiment

Materials

CH_2Cl_2 (Wako, super dehydrated grade) was dried over CaH_2 (Nacalai Tesque) and distilled under high vacuum just before use. Toluene (Aldrich, anhydrous grade) was dehydrated with red colored complex of butyllithium (*n*-BuLi, 1.64 M hexane solution, Kanto Chemical) and 1,1-diphenylethylene (Acros Organics), and distilled under high vacuum just before use. Ethylaluminum bis(2,6-di-*t*-butylphenoxide) [EtAl(ODBP)₂] and methylaluminum bis(2,6-di-*t*-butylphenoxide) [MeAl(ODBP)₂] were prepared according to our previous report⁴⁰ and stored as toluene solutions under nitrogen atmosphere. MMA (Nacalai Tesque), vinyl methacrylate (VMA, Tokyo Chemical Industry), and butyl acrylate (BA, Tokyo

Chemical Industry) were fractionally distilled and stored over CaH_2 . The monomers were distilled over CaH_2 under high vacuum just before use. Me_3SiOLi (Aldrich) was dried *in vacuo* at 100 °C for several hours and used as dry toluene or CH_2Cl_2 solution. The received reagent contains a significant amount of insoluble material, and thus the supernatant solution was used for polymerization. Isopropyl α -lithioisobutyrate (Li-*i*PrIB) was prepared and recrystallized in toluene according to our previous report.³² Ethyl α -(chloromethyl)acrylate (**1a**) and ethyl α -(bromomethyl)acrylate (**1b**) were synthesized from ethyl α -(hydroxymethyl)acrylate, a kind gift from Nippon Shokubai Co., Ltd, according to our previous report.³⁹ **1a** (bp 44.3–45.0 °C / 2.5 mmHg) and **1b** (bp 45.0–45.3 °C / 2.0 mmHg) were distilled under reduced pressure and stored under nitrogen atmosphere in the presence of Molecular Sieves 4A (MS4A, Nacalai Tesque) at -20 °C. Ethyl 2-methylpent-4-enoate (Aldrich) and diisopropylamine were dried over CaH_2 , distilled under high vacuum, and stored as toluene solutions. Benzylidene-bis(tricyclohexylphosphine)dichlororuthenium (first generation Grubbs' catalyst, Aldrich) and other reagents were used as purchased without further purification.

Instruments

¹H and ¹³C NMR spectra were measured in $CDCl_3$ (Aldrich) on a Unity Inova 500 spectrometer (Varian) and an ECS-400 spectrometer (JEOL). Chemical shifts in ¹H NMR spectra were referred to the signal of tetramethylsilane (TMS). Molecular weights and its distributions of the polymers were determined at 40 °C by size-exclusion chromatography (SEC) using a GPC-900 chromatograph (JASCO) equipped with two SEC columns [Polymer Laboratories, PL-gel, Mixed C (300 mm \times 7.5 mm)], using tetrahydrofuran (THF) as an eluent at a flow rate of 0.8 mL \cdot mL⁻¹, and calibrated against standard PMMA samples (Shodex, MW: 1.25×10^6 , 6.59×10^5 , 1.95×10^5 , 4.96×10^4 , 2.06×10^4 , 6.82×10^3 , 2.00×10^3).

Trimethylsilyl Methacrylate (TMSMA)

Under nitrogen atmosphere, chlorotrimethylsilane (100 mL, 0.790 mmol) was added dropwise to a suspension of potassium methacrylate (99.3 g, 0.800 mmol) in Et_2O (750 mL) containing MS4A (15 g). After 21 h, the precipitate was removed by filtration over Cerite® No. 535 (Wako), and the filtrate was concentrated. The residue was distilled twice under reduced pressure with Vigreux column (40.5 °C / 16 mmHg) to give TMSMA as colorless oil (70.7 g). Yield: 55.8%. Purity: 99.6%. $d = 0.8898$ g/cm³. ¹H NMR (400 MHz, $CDCl_3$, 30 °C) δ 6.09 (dd, $J_1 = 1.8$ Hz, $J_2 = 0.9$ Hz, 1H, $CHH=$), 5.58 (dd, $J_1 = 1.8$ Hz, $J_2 = 1.6$ Hz, 1H, $CHH=$), 1.91 (dd, $J_1 = 1.6$ Hz, $J_2 = 0.9$ Hz, 3H, α - CH_3), 0.31 (s, 9H, $SiMe_3$) ppm. ¹³C NMR (100 MHz, $CDCl_3$, 30 °C) δ 168.4 (C=O), 138.3 (α), 126.6 (β), 18.9 (OCH₃), 0.44 ($SiMe_3$) ppm.

Polymerization

All the polymerization reactions were carried out under dried nitrogen atmosphere in glass ampoules fitted with three-way stopcocks and the solvents and reagents were transferred via

hypodermic syringes. A typical procedure (Table 1, Run 2): To a glass ampoule filled in dried nitrogen passed through MS4A at $-78\text{ }^{\circ}\text{C}$, CH_2Cl_2 (5.0 mL), Me_3SiOLi (2.5 mmol), and $\text{Li-}i\text{PrIB}$ (0.25 mmol) were added at room temperature. The reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$, and the polymerization was started by the addition of MMA (5.0 mmol). After 1 h, **1a** (1.25 mmol) was added to the polymerization mixture and reacted for further 1 h. Then the reaction was finally quenched by HCl aq-MeOH solution, and the polymer was recovered by precipitation with hexane, filtered and washed with hexane, acidic water and water, successively, and dried *in vacuo* at $40\text{ }^{\circ}\text{C}$.

Thiol-ene 'click' reaction

A typical procedure: To a solution of *st*-PMMA (**st-2**, 64 mg, 20 μmol of the functional group) in CH_3CN (0.20 mL) was added a catalytic amount of (Et_3N) and **2b** (0.17 mL, 2.0 mmol). The reaction mixture was stirred at ambient temperature for 12 h and poured into hexane (30 mL). The precipitate was collected by centrifugation and washed with water, then dried *in vacuo* for 6 h to give the corresponding polymer (62 mg). For the PMMA with higher molar masses (**it-4**, **st-5**, and **st-6**), the volume of the solvent was 0.50 mL and the molar concentration of the functional group was 20 mM instead of 100 mM in the typical case described above.

ω -Functional stereoregular poly(methacrylic acid)

To a solution of *it*-poly(VMA) (**V1**, 74 mg, 10 μmol) in Et_3N (0.209 mL, 1.50 mmol) was added 2-mercaptoethylammonium chloride (**2d**, 0.113 g, 1.00 mmol). After 12 h, H_2O (30 mL) was added, and the product was extracted with CHCl_3 (30 mL). The organic layer was concentrated, and the residue was dried *in vacuo*. The obtained ω -functional polymer (70 mg, 0.63 mmol/unit) was dissolved in CF_3COOH (1.0 mL, 13 mmol) and H_2O (0.23 mL, 13 mmol). The reaction mixture was heated at $70\text{ }^{\circ}\text{C}$ for 3 h and poured into acetone (30 mL). The precipitate was collected by centrifugation and dried *in vacuo* to give a poly(methacrylic acid) (57 mg).

Amine-isocyanate 'click' reactions

st-PMMA (**st-13**) was reacted with 11-mercaptoundec-1-ene (**2g**) in a similar manner as described above. The product (40

mg, 12 μmol) was dissolved in CDCl_3 (0.60 mL) and Et_3N (18 μL , 120 μmol). 2-isocyanatoethyl methacrylate (**4a**, 17 μL , 120 μmol) was added, and the reaction was monitored by $^1\text{H NMR}$ spectroscopy. After 15 h, the reaction mixture was poured into hexane (50 mL). The precipitate was collected by centrifugation, dissolved in CHCl_3 (10 mL), washed with 1 M HCl aq (10 mL) and H_2O (10 mL), and concentrated. The residue was dried *in vacuo* to give a polymeric product (40 mg).

Thiol-ene and amine-isocyanate 'double click' reactions

S-(Undec-10-en-1-yl) acetothioate (0.25 mL, 1.0 mmol) was treated with propylamine (0.16 mL, 2.0 mmol) in CH_3CN (0.20 mL) at ambient temperature for 3 h, and *st*-PMMA (**st-14**, 64 mg, 20 μmol) was added. After 14 h, phenyl isocyanate (**4b**, 0.33 mL, 3.0 mmol) was added. After 12 h, the reaction mixture was diluted with CHCl_3 (1 mL) and poured into hexane (50 mL). The precipitate was collected by centrifugation, washed with hexane, and dried *in vacuo*. The precipitate was dissolved in CHCl_3 (1 mL), and insoluble product was removed by filtration. The solution was concentrated, and the residue was dissolved in acetone. The solution was poured into water (15 mL) – MeOH (35 mL) cosolvent, and the precipitate was collected by centrifugation and dried *in vacuo* at $40\text{ }^{\circ}\text{C}$ to give a polymeric product (16 mg).

Synthesis of telechelic *it*-PMMA (**it-7m**)

All reagents were added via hypodermic syringes. To a glass ampoule filled in dried nitrogen gas passed through MS4A at $-78\text{ }^{\circ}\text{C}$, to a solution of *n*-BuLi in hexane (1.64 M, 0.24 mL, 0.40 mmol) was added diisopropylamine in toluene (0.98 M, 0.24 mL, 0.46 mmol) was added dropwise. After 1 h, ethyl 2-methylpent-4-enoate in toluene (0.75 M, 0.53 mL, 0.40 mmol) was added to the viscous reaction mixture cooled over water bath. After 1 h, Me_3SiOLi in toluene (0.99 M, 2.0 mL, 2.0 mmol) and toluene (2.0 mL) was added, and the reaction mixture was cooled at $-78\text{ }^{\circ}\text{C}$. MMA (1.1 mL, 10 mmol) was added to initiate the polymerization. After 30 min, the reaction mixture was warmed at $-30\text{ }^{\circ}\text{C}$, and **1a** (1.3 mL, 1.0 mmol) was added. The reaction was finally quenched by 5 M HCl aq (0.7 mL). The reaction mixture was then poured into hexane (150 mL), and the precipitate was collected by centrifugation and dried *in vacuo* to afford the product (1.36 g). It was dissolved in

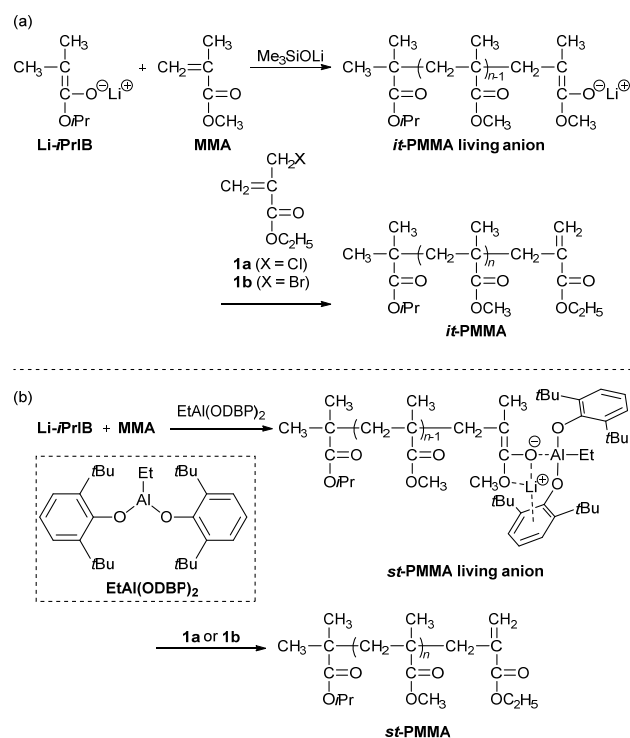
Table 1. Terminating reaction with α -(halomethyl)acrylates in isotactic-specific anionic polymerization of MMA.^a

Run	Polymerization		Termination				Polymer	Tacticity /%					
	$[\text{MMA}]_0 / [\text{Li-}i\text{PrIB}]_0$	Solvent	T^b	Equiv. ^c	Temp./ $^{\circ}\text{C}$	Time/ h		M_n^d	M_w/M_n^d	<i>mm</i>	<i>mr</i>	<i>rr</i>	$F^f / \%$
1	20/1	CH_2Cl_2	H_3O^+	excess	-78	>0	it-1	8000	1.22	98	2	~ 0	–
2	20/1	CH_2Cl_2	1a	5.0	-78	1	it-2	7000	1.18				90
3	20/1	CH_2Cl_2	1a	5.0	-40	1	it-3	6800	1.19				93
4	100/1	CH_2Cl_2	1a	5.0	-78	1	it-4	28000	1.32	97	3	~ 0	93
5	20/1	CH_2Cl_2	1b	5.0	-78	1	it-5	8000	1.20				93
6	20/1	Toluene	1b	5.0	$-78 \rightarrow 0^e$	1	it-6	7500	1.26				96

^a Polymerizations of MMA (5.0 mmol) were carried out in solvent (5.0 mL) at $-78\text{ }^{\circ}\text{C}$ for 1 h. $[\text{Me}_3\text{SiOLi}]_0 / [\text{Li-}i\text{PrIB}]_0 = 10 / 1$. ^b Terminating agent.

^c Equivalent of terminating agent to $\text{Li-}i\text{PrIB}$. ^d Determined by SEC (PMMA standards). ^e Estimated by $^1\text{H NMR}$ spectra. ^f End-functionalization efficiency

^g Terminating agent was added at $-78\text{ }^{\circ}\text{C}$ and then the reaction system was warmed to $0\text{ }^{\circ}\text{C}$.



Scheme 1. Termination of (a) *it*- or (b) *st*-PMMA living anions with **1**.

CHCl_3 and washed with 1 M HCl aq (20 mL) twice and H_2O (20 mL). The organic layer was concentrated and dried *in vacuo* to recover the product (**it-7**, 0.83 g). The obtained *it*-PMMA (**it-7m**) was reacted with **2g** in a similar manner described above to give a telechelic *it*-PMMA.

Attempt of cyclization telechelic *it*-PMMA by olefin-metathesis reaction

The telechelic *it*-PMMA obtained above (57mg, 10 μmol) was dissolved in anhydrous CH_2Cl_2 (100 mL) distilled over CaH_2 under vacuum. First generation Grubbs' catalyst (19 mg, 20 μmol) was added to the solution, and the reaction mixture was refluxed for 5 days, passed through activated alumina layer, and concentrated to give the product (37 mg).

Results and Discussion

Terminating reaction of *it*-PMMA living anion

According to the previous report,³² isotactic-specific living polymerization of MMA was carried out in CH_2Cl_2 at -78°C with Li-*i*PrIB / Me_3SiOLi (Scheme 1a). After 1 h, the conversion of MMA reached 100%, and terminating agents, HCl aq—MeOH solution (Table 1, Run 1) or **1a** (Run 2) were added. Fig. 1 shows the ^1H NMR spectra of the resulting polymers, **it-1** and **it-2**. In both cases, the isotacticity (*mm* contents), determined from the integral ratio of $\alpha\text{-CH}_3$ signals were higher than 98%. In the ^1H NMR spectrum of **it-1** (Fig. 1a), the signal assignable to CH proton at ω -end was observed around 2.44 ppm. In contrast, the $\omega\text{-CH}$ signal was very weak in the ^1H NMR spectrum of **it-2**, while the signals assignable to

vinylidene (6.17 and 5.48 ppm), *O*-methylene (4.17 ppm), and allylic (2.62 and 2.47 ppm) protons were observed (Fig. 1b), which clearly indicate the presence of an α,β -unsaturated ethyl ester unit, supporting effective terminating reaction with **1a** to afford *it*-PMMA with ω -end C=C bond. The end-functionalization ratio (*F*) was determined as 90% from the intensity ratio of the vinylidene signals at ω -end to the CH signal of isopropyl ester at α -end. Termination at higher temperature (-40°C) did not significantly improve the end-functionalization ratio (*F* = 93%, Run 3). The terminating reaction was proved effective for an *it*-PMMA anion with higher molecular weight (Run 4: $M_n = 28000$, $M_w/M_n = 1.32$, *F* = 93%). The bromide **1b** also gave a similar result (Run 5: *F* = 93%), indicating the leaving ability of halogen atom is not significant in the terminating reaction. In contrast to the polymerization in CH_2Cl_2 , the polymerization in toluene at -78°C resulted in gelation of the reaction mixture. Thus, the reaction mixtures were gradually heated up to 0°C after the addition of the terminating agents at -78°C in order to mix them homogeneously. Though the living *it*-PMMA anion may undergo spontaneous chain-end cyclization termination at 0°C , the end-functionalization ratio was even higher (Run 6: *F* = 96%). Consequently, the efficiency of terminating reaction is not significantly dependent on the reaction conditions.

Terminating reaction of *st*-PMMA living anion

In a similar way, syndiotactic specific living polymerization of MMA was carried out in CH_2Cl_2 at -78°C with a binary initiator, Li-*i*PrIB / EtAl(ODBP)_2 for 24 h (Conv. $\sim 100\%$) and terminated with HCl aq—MeOH solution (Table 2, Run 7) or **1a** (Run 8) to give the corresponding polymers, **st-1** and **st-2**, respectively (Scheme 1b). Fig. 2 shows the ^1H NMR spectra of **st-1** and **st-2**. In both cases, syndiotacticity determined from the

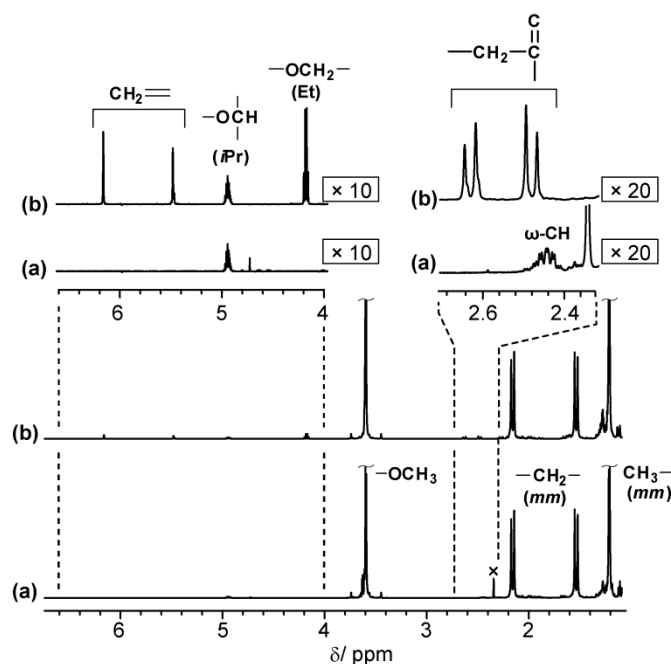


Fig. 1 ^1H NMR spectra of (a) **it-1** and (b) **it-2** (500 MHz, CDCl_3 , 55°C). \times : toluene.

Table 2. Terminating reaction with α -(halomethyl)acrylates in syndiotactic-specific anionic polymerization of MMA.^a

Run	Polymerization		Termination				Polymer	Molecular Weight		Tacticity /%			
	[MMA] ₀ / [Li- <i>i</i> PrIB] ₀	Solvent	T ^b	Equiv. ^c	Temp./ °C	Time/ h		M _n ^d	M _w /M _n ^d	<i>mm</i>	<i>mr</i>	<i>rr</i>	F ^f / %
7	20/1	CH ₂ Cl ₂	H ₃ O ⁺	excess	-78	>0	st-1	2800	1.06	~0	13	87	–
8	20/1	CH ₂ Cl ₂	1a	5.0	-78	1	st-2	3200	1.06				98
9	20/1	CH ₂ Cl ₂	1a	5.0	-78	5	st-3	2600	1.06				99
10	20/1	CH ₂ Cl ₂	1a	5.0	-40	1	st-4	3300	1.06				91
11	100/1	CH ₂ Cl ₂	1a	5.0	-78	1	st-5	11300	1.08	~0	11	89	100
12	200/1	CH ₂ Cl ₂	1a	5.0	-78	1	st-6	23700	1.07	~0	9	91	99
13	20/1	CH ₂ Cl ₂	1a	0.50	-78	1	st-7	3200	1.06				80
14	20/1	CH ₂ Cl ₂	1a	3.0	-78	1	st-8	3100	1.06				100
15	20/1	CH ₂ Cl ₂	1b	5.0	-78	1	st-9	3000	1.08				99
16	20/1	Toluene	1b	5.0	-78	1	st-10	2100	1.12				95
17	20/1	Toluene	1b	5.0	-78→0 ^g	1	st-11	2100	1.14				98

^a Polymerizations of MMA (5.0 mmol) were carried out in solvent (5.0 mL) at -78 °C for 24 h. ^b Terminating agent. ^c Equivalent of terminating agent to Li-*i*PrIB. ^d Determined by SEC (PMMA standards). ^e Estimated by ¹H NMR spectra. ^f End-functionalization efficiency. ^g Terminating agent was added at -78 °C and then the reaction system was warmed to 0 °C.

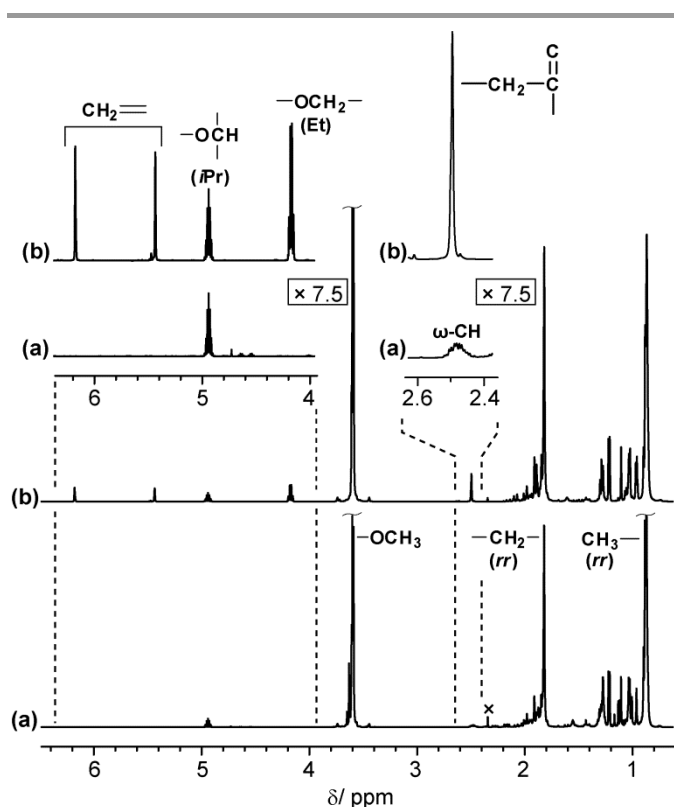


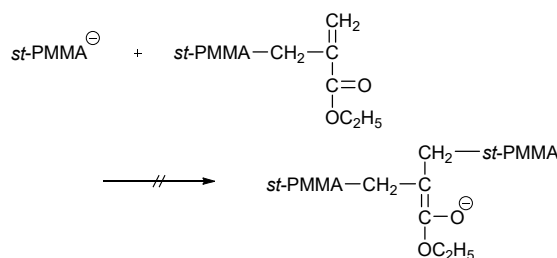
Fig. 2. ¹H NMR spectra of (a) **st-1** and (b) **st-2** (500 MHz, CDCl₃, 55 °C). ×: toluene.

α -CH₃ signals were high (*rr* content = 87%). As in the case of *it*-PMMA, the ¹H NMR spectrum of **st-1** (Fig. 2a) exhibits the ω -CH signal (2.48 ppm), while that of **st-2** (Fig. 2b) showed the vinylidene (6.17 and 5.48 ppm), *O*-methylene (4.17 ppm), and allylic protons (2.52 ppm), indicating the smooth terminating reaction of *st*-PMMA with **1a** ($F = 98\%$). Bulky aluminum bisphenoxides like EtAl(ODBP)₂ are known to form complexes with lithium ester enolate.⁴¹ In this polymerization system, therefore, the living enolate anion may strongly interact with EtAl(ODBP)₂ to be stabilized so as to afford livingness (Scheme 1b).⁵² Although this ate-complex type propagating

species have lower reactivity than free enolate anion, almost quantitative end-functionalization was achieved by the termination with **1a** ($F = 98\%$).

The terminating reaction seemed to complete within 1 h (Run 8: $F = 98\%$), and the F value slightly increased after 5 h (Run 9: $F = 99\%$). The termination at -40 °C resulted in lower F value (Run 10: $F = 91\%$), although the reason was not clear. On the other hand, molecular weight did not affect the end-functionalization (Runs 11, 12). Although the polymerization in toluene became highly viscous even when the M_n of the obtained PMMA was 2100, the termination with **1b** (Runs 16, 17) gave similar results to that in CH₂Cl₂ (Run 15).

The effect of amounts of added **1a** was also investigated (Runs 8, 13, 14). It was found that the addition of 1.0 equiv. of **1a** to initiator (Li-*i*PrIB) was enough to terminate the polymerization quantitatively (Run 14). It should be noted that the initiator efficiency was ~67% in this polymerization so that 1.0 equiv. of **1a** was excess to the living anions. In fact, the addition of 0.50 equiv. of **1a** resulted in $F = 80\%$ as the case of Run 13. When the F value is significantly lower than unity, the living PMMA remained might attack the ω -end C=C bond of the terminated PMMA to form higher molecular weight product (Scheme 2). The SEC trace of **st-7** was unimodal distribution with a molecular weight dispersity ($M_w/M_n = 1.06$) as small as the other Runs. Thus, such a reaction did not occur, probably due to the bulkiness of PMMA chain attached to the C=C bond, since the bulkiness of α -substituent in α -substituted acrylate drastically decreases the reactivity of vinylidene group.



Scheme 2. Chain-transfer reaction to the generated C-C bond at ω -end.

Table 3. Terminating reaction with **1a** in stereospecific polymerization of various (meth)acrylates initiated by Li-*i*PrIB.^a

Run	Polymerization				Termination		Polymer	M_n^c	M_w/M_n^c	Tacticity /% ^d				$F^{d,e} / \%$
	Monomer (equiv.) ^b	Additive (equiv.) ^b	Solvent	Temp. / °C	Time /h	Temp. /°C				Time /h	mm	mr	rr	
18	VMA (20)	Me ₃ SiOLi (10)	Toluene	-78	1	-78	1	V1	7400	1.08	98	2	~0	98
19	VMA (20)	EtAl(ODBP) ₂ (3.0)	Toluene	-78	24	-78 → -30 ^e	1	V2	4700	1.05	~0	13	87	98
20	TMSMA (50)	Me ₃ SiOLi (10)	CH ₂ Cl ₂	-78	1	-78	1	TMS1	14000	1.46	94	4	2	94
21	TMSMA (50)	MeAl(ODBP) ₂ (3.0)	CH ₂ Cl ₂	-78	24	-78 → 0 ^f	24	TMS2	2500	1.09	1	3	96	96
22	BA (50)	EtAl(ODBP) ₂ (5.0)	Toluene	-60	0.5	-60	1	B1	10800	1.16				69

^a Solvent = 5.0 mL, monomer = 5.0 mmol, [Li-*i*PrIB]₀ / [**1a**]₀ = 1 / 5. ^b Equivalent against Li-*i*PrIB. ^c Determined by SEC (THF, PMMA standards). ^d Estimated by ¹H NMR spectroscopy (500 MHz, CDCl₃, 55 °C). ^e End-functionalization efficiency. ^f The reaction mixture was warmed to -30 °C / 0 °C then stirred for 1 h / 24 h.

Terminating reaction with other (meth)acrylates

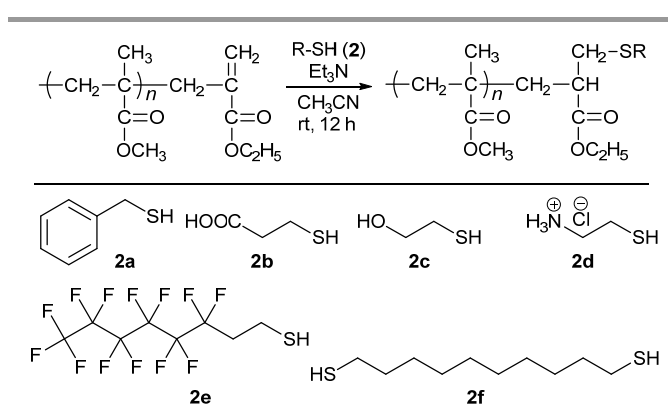
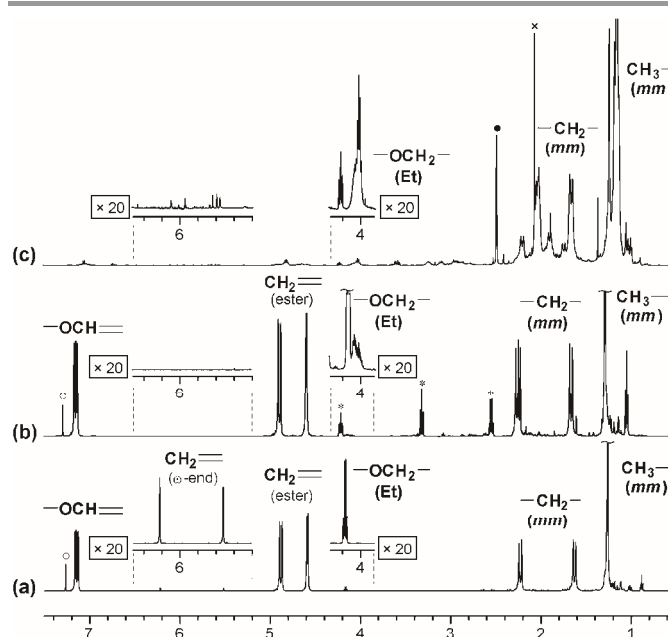
The terminating reaction with **1a** was applied to other (meth)acrylate monomers in order to reveal the applicable scope (Table 3). Although the stereospecific anionic polymerizations of *sec*-alkyl methacrylates such as isopropyl methacrylate are known not to be controllable well, we recently have found that of VMA can be controlled.⁴² Both in isotactic- (Run 18) and syndiotactic- (Run 19) specific polymerizations of VMA, the terminating efficiencies with **1a** were almost quantitative ($F = 98\%$). Although the stereospecific polymerizations of *tert*-alkyl esters, *i.e.* *tert*-butyl methacrylates, in the above mentioned conditions are not controllable, those of TMSMA have been established.⁴³ Isotactic- and syndiotactic-specific polymerization of TMSMA was terminated with high efficiencies (Runs 21, 22). Since the polymerization was finally quenched with HCl aq, the products were obtained as poly(methacrylic acid) due to the acid-hydrolysis of silyl ester.

As reported, polymerization of BA in the presence of EtAl(ODBP)₂ proceeds in a living manner.⁴⁹ Thus, the termination with **1a** was also applied to this polymerization system (Run 22). However, the terminating efficiency was not quantitative ($F = 69\%$). This might be due to the low reactivity of the living polyacrylate anion (*secondary* carbanion) than that of polymethacrylate anion (*tertiary* carbanion), and further optimization of the conditions for the terminating reaction is under examination.

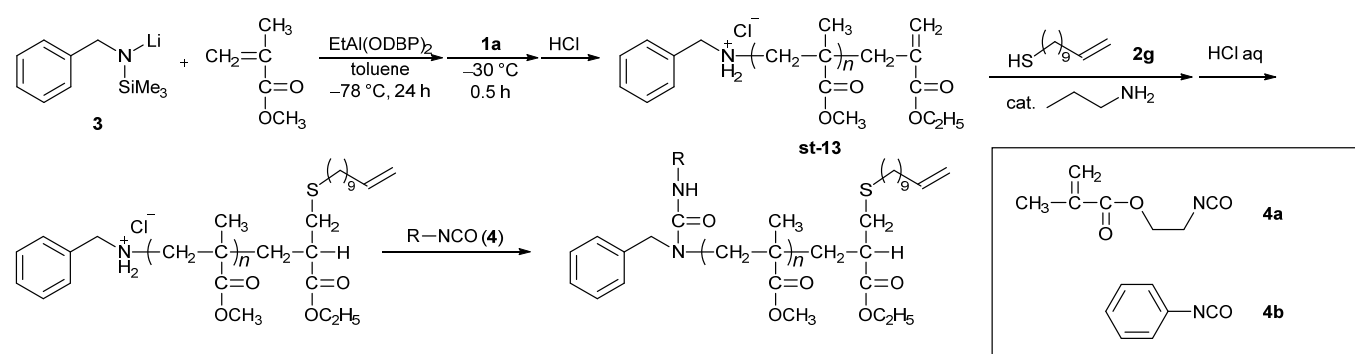
Stereoregular PMMA and poly(methacrylic acid) with ω-functions via post-polymerization modification

As the C=C double bond at the ω-end is activated by the carbonyl group, it can undergo Michael-addition type thiol-ene click chemistry. In fact, we previously reported the further functionalizations of the end-functional stereoregular PMMAs with various thiols (**2a-d**) (Scheme 3). In a similar way, end-functionalization was attempted for other thiols and polymers.

Sugiyama *et al.* have reported that the chain-end modification of polymethacrylates with a perfluoroalkyl group improves their water-repellency.⁴⁵ Thus, thiol possessing perfluoroalkyl group, **2e**, was reacted with *st*-PMMA in ethyl acetate at 50 °C. Although the reaction mixture became heterogeneous, the conversion of terminal vinylidene group reached 92% after 48 h. The reaction was then repeated again, and the conversion finally increased to 95%. Bifunctional thiol

**Scheme 3.** End-functionalization by thiol-ene 'click' chemistry.**Fig. 3.** ¹H NMR spectra of **V1** (a) before and (b) after thiol-ene reaction with **2d** in CDCl₃, and (c) the hydrolysis product [poly(methacrylic acid)] in DMSO-*d*₆ (500 MHz, 55 °C). ○: CHCl₃, ●: DMSO, *: residual **2d**, ×: acetone.

(**2f**) was also reacted to the terminal vinylidene group in order to incorporate thiol group at the ω-end. To suppress the dimerization, a large excess (50-fold) of **2f** was reacted with *st*-PMMA (**st-4**). Since the SEC profile of the obtained polymer agreed with its precursor, no dimerization occurred under this



Scheme 4. Synthesis and double click reaction of hetero-telechelic *st*-PMMA.

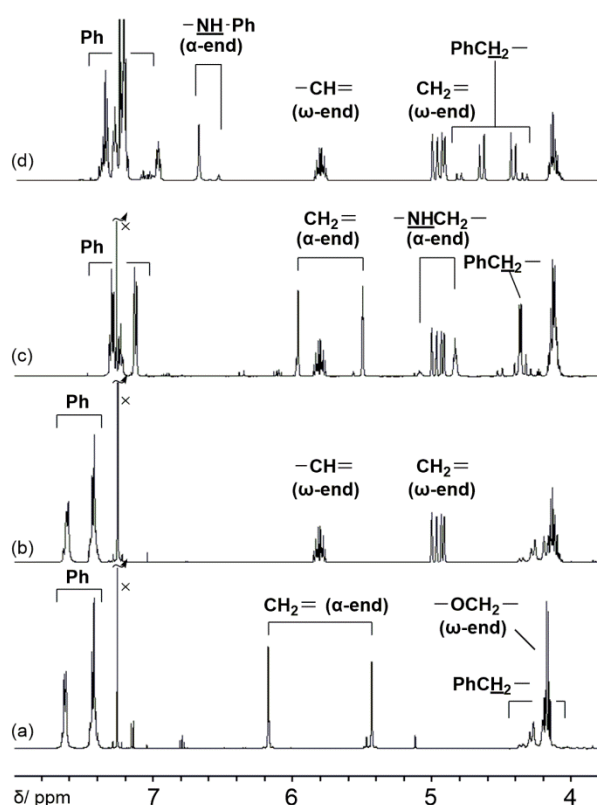


Fig. 4. ¹H NMR spectra of **st14** (a) before and (b) after thiol-ene reaction with **2g**, and (c) the product after amine-isocyanate reaction with **4a** and that with **4b** (500 MHz, CDCl₃, 55 °C). x: CHCl₃.

condition.

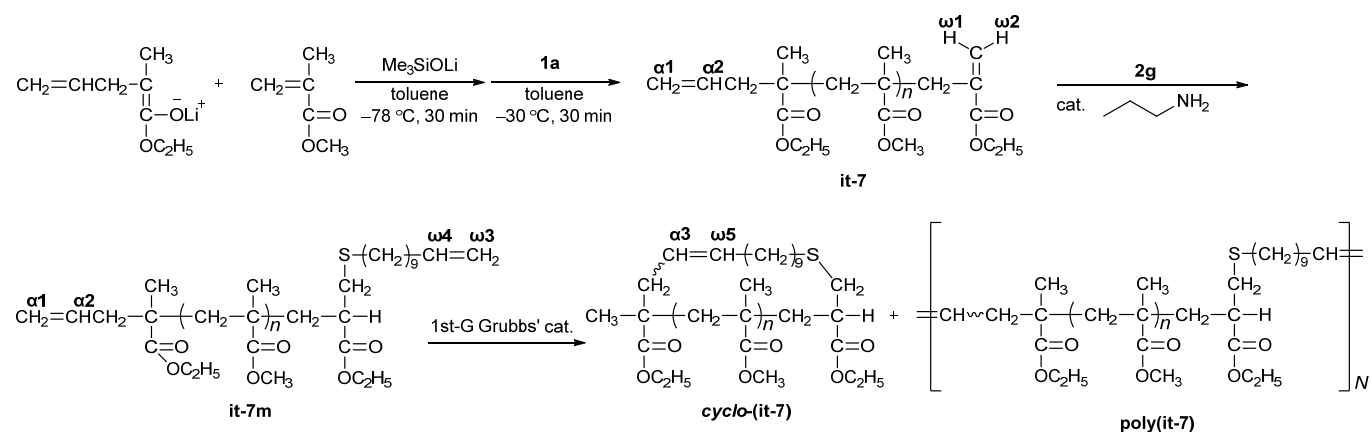
The effect of molecular weight on the thiol-ene ‘click’ reactions was also investigated with **it-4** ($M_n = 28000$), **st-5** ($M_n = 11300$), and **st-6** ($M_n = 23700$). Due to the higher molecular weight of these polymers, the concentration of the functional group was set to be 20 mM instead of 100 mM in the previous cases, where the reaction mixtures were even more viscous. Nevertheless, quantitative end-functionalization was achieved without any further experimental modification such as reaction period and temperature.

In the case of poly(VMA), the vinylidene group at the ω -end is activated by the carbonyl group enough to allow the Michael-addition of thiol, while the vinyl ester groups in the monomeric units are inactive against the Michael-addition. Thus, the orthogonal and stepwise modifications of the vinylidene and vinyl groups are possible. Treatment of *it*-poly(VMA) (**V1**) with **2d** in the presence of Et₃N afforded an amine-functionalized polymer. In ¹H NMR spectra (Fig. 3), the vinylidene signals (6.22 and 5.52 ppm) completely disappeared, while the vinyl ester signals (7.15, 4.88, and 4.59 ppm) did not change. Then the end-functionalized polymer was hydrolyzed with CF₃COOH. The obtained polymer did not show the vinyl signals. Consequently, the synthesis of end-functional stereoregular poly(methacrylic acid) was achieved.

Stereoregular PMMA with orthogonally-clickable α - and ω -ends

Recently, polymer architectures by orthogonal double click reactions at both ends have gained much attention.⁴⁶ We have previously reported that a silyl-protected lithium amide initiator (**3**) in combination with aluminum compounds was effective for syndiotactic-specific polymerization of MMA, which allows the incorporation of a secondary amino group at the α -end of PMMA.³⁷ As well known, a secondary amino group can be applied to click chemistry through urea-formation with an isocyanate. Hence, a combination of **3** as a functional initiator and **1a** as an efficient terminating agent may afford hetero-telechelic *st*-PMMA with orthogonally-clickable ends (Scheme 4). In fact, the anionic polymerization gave *st*-PMMA (**st-13**: $M_n = 3200$, $M_w/M_n = 1.06$, $mm/mr/rr = 0/13/87$, $F = 98\%$).

11-Mercaptoundec-1-ene (**2g**) was prepared *in situ* from the corresponding thioester with propylamine and reacted with **st-13**. Fig. 4 shows the ¹H NMR spectral changes after the reaction. Apparently, the signals of vinylidene protons due to the ω -end group disappeared and those of vinyl protons derived from **2g** were observed, indicating the complete thiol-ene click reaction. Subsequently, the product was reacted with 2-isocyanatoethyl methacrylate (**4a**). Fig. 4c shows the shift of signals assignable to aromatic protons and the appearance of new signals assignable to the vinylidene protons (5.50 and 5.97 ppm) and that of the urea proton (4.27-4.57 ppm). These



Scheme 5. Synthesis and olefin-metathesis reaction of telechelic *it*-PMMA.

spectral changes indicated that the second click reactions proceeded completely without any side reactions. Furthermore, one-pot double-click reactions were investigated by using phenyl isocyanate (**4b**) in place of **4a** to avoid a side reaction of the unreacted thiol to **4a**. After the first click reaction with **2g**, an excess amount of **4b** was added. ^1H NMR spectral changes similar to the stepwise click reactions were observed (Fig. 4d), and thus it is concluded that quantitative double end-functionalization was achieved via orthogonal double click reactions.

Attempted synthesis of cyclic polymer

Recently, Kamigaito *et al.* have reported that cyclic (*cyclo*-)*st*-PMMA forms polypseudorotaxane with *it*-PMMA.⁴⁷ Inspired by this work, we have attempted the synthesis of *cyclo-it*-PMMA from a telechelic PMMA with vinyl groups at the both ends by olefin-metathesis reaction.^{48,49} The telechelic *it*-PMMA (**it-7m**) was prepared through two step reactions; an isotactic-specific polymerization of MMA was initiated by a lithium enolate of ethyl 2-methylpent-4-enoate and terminated with **1a** to afford **it-7** ($M_n = 5100$, $M_w/M_n = 1.24$, $F = 96\%$, $mm/ mr/ rr = 96 / 4 / 0$), followed by the thiol-ene reaction with **2g** (Scheme 5). The obtained telechelic polymer, **it-7m**, was refluxed with the first generation Grubbs' catalyst in CH_2Cl_2 (1.0×10^{-4} M) for 4 days. In ^1H NMR spectra (Fig. 5), the vinylidene signals ($\omega 1$: 6.16 ppm, $\omega 2$: 5.48 ppm) disappeared and after the thiol-ene reaction, and new vinyl proton signals ($\omega 2$: 5.85-5.77, $\omega 1$: 5.03-5.00 ppm) appeared, indicating the quantitative end-functionalization. These end-group signals disappeared almost completely after the olefin-metathesis reaction, while new olefinic proton signals ($\alpha 3/\omega 5$: 5.82-5.71 and 5.14-5.07 ppm) assignable to the generated vinylene group appeared, indicating the high efficiency of metathesis reaction. However, the increase in molecular weight (peak top: $M_p = 67000$) from the precursor ($M_p = 7700$) was observed in the SEC trace of the product, although a small second peak at lower molecular weight ($M_p = 6700$) was also seen (Fig. 6). The former peak indicates the polycondensation of **it-7**, and the resulting polymer [**poly-(it-7)**] was estimated as *ca.* 9 mer of **it-**

7 in average from the increase in M_p . The latter peak is presumably a targeted cyclic polymer, [**cyclo-(it-7)**], since the

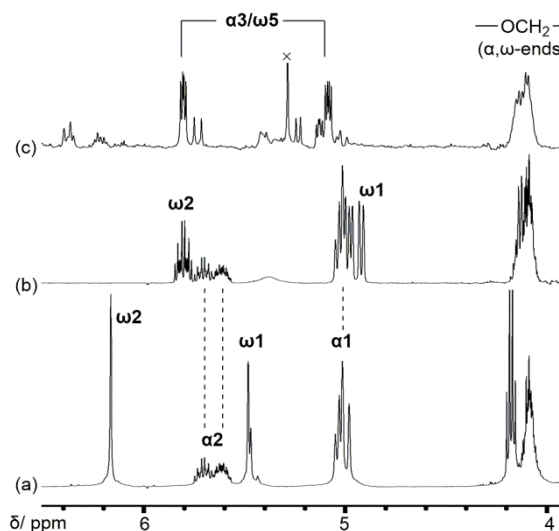


Fig. 5. ^1H NMR spectra of **it-7** (a) before and (b) after thiol-ene reaction with **2g**, and (c) after olefin-metathesis reaction (500 MHz, CDCl_3 , 55°C). \times : CH_2Cl_2 . For notations of end-groups, refer to Scheme 5.

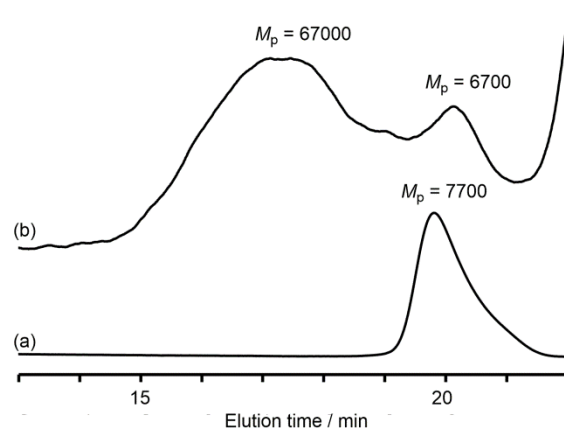


Fig. 6. SEC traces of **it-7m** (a) before and (b) after olefin-metathesis.

M_p was 0.87 times of the precursor as expected from smaller hydrodynamic volume of a cyclic polymer than the respective linear polymer.^{49,50}

Conclusions

Stereoregular ω -functional PMMAs were synthesized by the combination of terminating reactions of stereospecific living anionic polymerizations and click chemistry. α -(Halomethyl)acrylates were highly active in terminating reaction of PMMA living anion so that almost quantitative end-functionalization was achieved. The terminating reaction was found to proceed with high efficiency in the polymerization of VMA and TMSMA. The incorporated C=C double bond underwent Michael addition of functional thiols to allow further end-functionalizations. This reaction was also possible for poly(VMA), which afforded the ω -functional poly(methacrylic acid) after hydrolysis. The combination of functional initiator and the terminating agent resulted in hetero-telechelic PMMAs, which allowed orthogonal double-click reactions at the both ends.

One of the goals of precise polymerization chemistry is simultaneous control of primary structures of macromolecules such as molecular weight, configuration and end-functionality. The above results are the successful example of them with highly sophisticated level in the polymerization of methacrylates. Nowadays, the growth of needs for end-clickable polymer has drastically increased not only in polymer chemistry but also in the fields of material science and medical science, as the concept of 'click chemistry' has become a robust, facile, and efficient methodology for chemical ligation in those areas. The current results may be a bridge builder between two concepts, stereospecific anionic polymerization and end-clickable polymer, and promote the use of a stereoregular polymers as building blocks at an edge of polymer science.

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Notes and references

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