

Main-Chain and Side-Chain Sequence-Regulated Vinyl Copolymers by Iterative Atom Transfer Radical Additions and 1:1 or 2:1 Alternating Radical Copolymerization

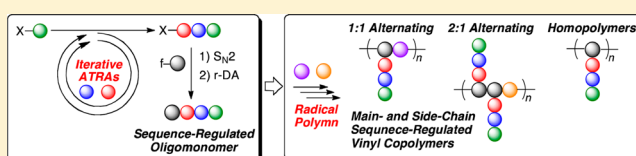
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S Supporting Information

ABSTRACT: Main- and side-chain sequence-regulated vinyl copolymers were prepared by a combination of iterative atom transfer radical additions (ATRA) of vinyl monomers for side-chain control and 1:1 or 2:1 alternating radical copolymerization of the obtained side-chain sequenced “oligomonomers” and vinyl comonomers for main-chain control. A complete set of sequence-regulated trimeric vinyl oligomers of styrene (S) and/or methyl acrylate (A) were first synthesized via iterative ATRA of these monomers to a halide of monomeric S or A unit (X–S or X–A) under optimized conditions with appropriate ruthenium or copper catalysts, which were selected depending on the monomers and halides. The obtained halogen-capped oligomers were then converted into a series of maleimide (M)-ended oligomonomers with different monomer compositions and sequences (M–SSS, M–ASS, M–SAS, M–AAS, M–SSA, M–ASA, M–SAA, M–AAA) by a substitution reaction of the halide with furan-protected maleimide anion followed by deprotection of the furan units. These maleimide-ended oligomonomers were then radically copolymerized with styrene or limonene to enable the 1:1 or 2:1 monomer-sequence regulation in the main chain and finally result in the main- and side-chain sequence-regulated vinyl copolymers with high molecular weights in high yield. The properties of the sequence-regulated vinyl copolymers depended on not only the monomer compositions but also the monomer sequences. The solubility was highly affected by the outer monomer units in the side chains whereas the glass transition temperatures were primarily affected by the two successive monomer sequences.



INTRODUCTION

Natural macromolecules such as proteins and nucleic acids possess perfectly ordered molecular structures in terms of chain lengths, stereostructures, and monomer sequences, which are essential for their special and unique functions.¹ Although synthetic macromolecules or polymers are widely used in our life, their primary structures are not perfectly controlled unlike natural ones. Most of these synthetic polymers are prepared via statistically governed successive chemical reactions, i.e., polymerization, which usually do not have perfect selectivity compared to biosynthesis. However, many efforts have been made to control the polymer structures more precisely because this is expected to contribute to improving polymer properties and providing new functions to the resulting polymers.^{2,3} The control of molecular weights and stereochemistry has thus become possible at sufficient levels, although not perfectly, through recent remarkable developments of various living polymerizations and stereospecific polymerizations, in which selective propagations are achieved in terms of chemoselectivity and stereoselectivity, respectively.

Monomer-sequence control in synthetic polymers remains one of the most challenging topics in polymer chemistry.^{4–48} One strategy for controlling monomer sequences in synthetic polymers is to develop highly comonomer-selective reactions,

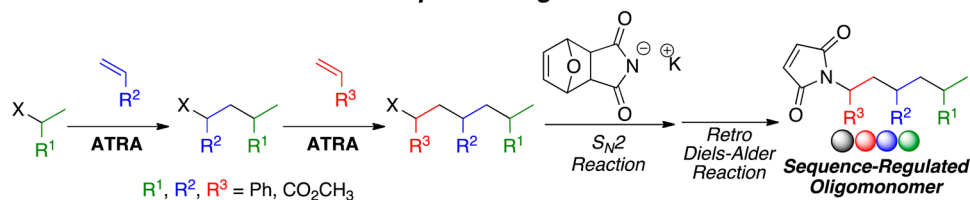
which can discriminate the comonomers by subtle differences in their structures and/or reactivities during the polymerizations. Another is to repeat the propagation reactions one by one iteratively by artificially adding one monomer and then another in the desired orders.

One of the most successful achievements based on the latter approach might be solid phase synthesis using Merrifield's resins along with the automation process,⁴⁹ which enables the perfectly controlled monomer sequence for artificial peptide and DNA. In view of the polymerization, this could be regarded as a kind of chain-growth process in which the reactions occur between the injected monomer and the attached polymer chain on the resin. Such one-by-one iterative methods can also be valid for a step-growth process in which the reactions occur first between the monomers and then between the resulting oligomers and polymers. The representative might be iterative exponential growth via stepwise reaction,^{50,51} which has recently been developed into a semiautomated flow system and enables the synthesis of a large amount of single molecular weight polymers consisting of sequence-regulated repeating units.^{52,53} Another successful achievement in synthesizing

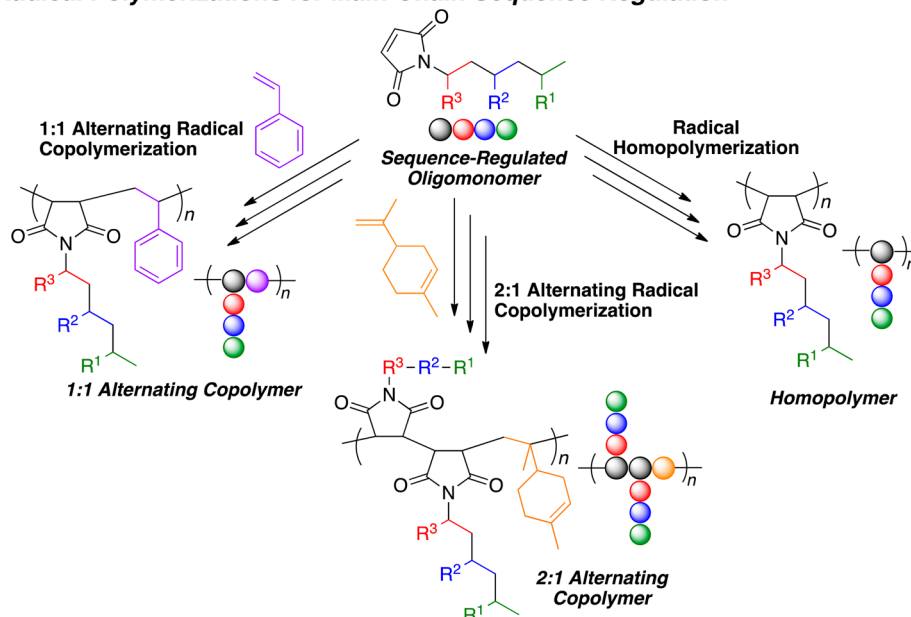
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Scheme 1. Synthesis of Sequence-Regulated Oligomonomers and Their Alternating 1:1 and 2:1 Radical Copolymerization and Homopolymerization for Main- and Side-Chain Sequence-Regulated Vinyl Copolymers

Iterative ATRAs for Side-Chain Sequence Regulation



Radical Polymerizations for Main-Chain Sequence Regulation



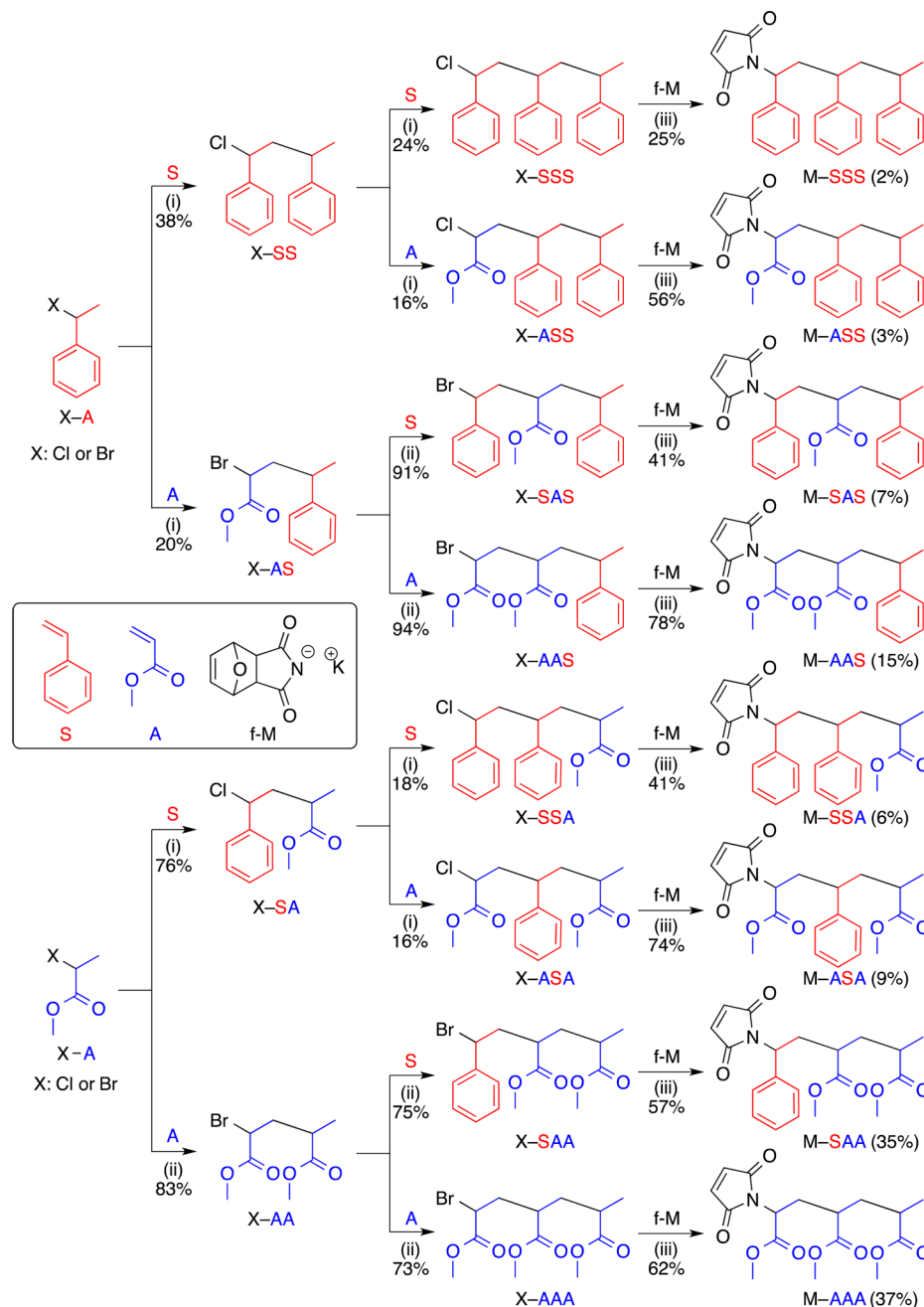
discrete and sequence-defined macromolecules might be the development of dendrimers via iterative methods including divergent and convergent approaches.^{54–56} In principle, these iterative methods enable the nearly perfect construction of the polymers but are unsuitable for very high-molecular-weight polymers because the yields must decrease with the successive reactions. The synthesis of sequence-regulated vinyl copolymers has especially been considered to be very difficult by the iterative methods.

With regard to the other strategy that will be achieved by developing highly comonomer-selective reactions, there might be various approaches, e.g., using differences in the comonomer reactivities, additives that can preferentially interact with one comonomer to alter the reactivity, or templates that can arrange the comonomers in desired orders during the reaction. In chain-growth radical copolymerizations for some pairs of monomers, such as styrene and cyclic maleic compounds, a 1:1 or AB alternating monomer sequence can be attained by the highly ordered statistics originating from the specific comonomer reactivity ratios.^{57,58} Furthermore, we have recently succeeded in a higher regulation such as 1:2 or ABB sequence in radical copolymerization of limonene and maleimide derivatives in some specific solvent that can alter the reactivity of comonomers.^{22–25} Although higher-ordered monomer sequencing is basically difficult in chain-growth copolymerizations, the chemically ordered selective reaction can easily provide high-molecular-weight polymers in high yield.

In this study, we took advantage of two strategies: artificially iterative addition reactions for making a perfect monomer sequence in the short side chains and chemically induced comonomer-selective chain-growth copolymerization for making the high-molecular-weight polymers with controlled main-chain sequences in high yield. For this, we used two reactions: iterative atom transfer radical additions (ATRAs) of vinyl monomers for sequencing the comonomers in the side-chains and AB or AAB-sequenced chain-growth radical copolymerization for ordering the monomer sequences in the long main chains of the high-molecular-weight vinyl copolymers.

ATRA or Kharasch addition reaction is not only recognized as a highly efficient radical addition reaction to produce well-defined organic molecules^{59,60} but is also extended to chain-growth polymerization as atom transfer radical polymerization (ATRP) or metal-catalyzed living radical polymerization.^{61–67} The polymerization is effective for regulating the molecular weights via reversible activation of the dormant carbon–halogen bonds by the metal catalysts and is widely used for the synthesis of various well-defined polymers such as block, end-functionalized, and star polymers. In addition, multiblock copolymers consisting of sequence-regulated polymeric or oligomeric blocks can be produced^{68–71} similar to other controlled/living radical polymerizations such as reversible addition–fragmentation chain transfer (RAFT) polymerization.⁷² However, the ATRP process itself cannot regulate the monomer sequence in the copolymerization because the comonomer reactivity ratio is in principle the same as that in conventional radical copolymerization.

Scheme 2. Synthesis of a Series of Maleimide-Ended Sequence-Regulated Oligomonomers (M-SSS, M-ASS, M-SAS, M-AAS, M-SSA, M-ASA, M-SAA, M-AAA) by Iterative ATRAs with (i) $\text{RuCp}^*\text{Cl}(\text{PPh}_3)_2$ or (ii) $\text{CuBr}/\text{PMDETA}$ and (iii) $\text{S}_\text{N}2$ Reactions Followed by Retro Diels–Alder Reactions^a



^aThe values in percentages below arrows and in parentheses indicate yields for each reaction and total yields of final products, respectively.

We have recently used single ATRAs iteratively between vinyl monomers via one-by-one addition for the synthesis of sequence-regulated telechelic oligomers with the reactive C—Cl bond at one end and the nonconjugated C=C bond at the other.²⁶ The obtained telechelic oligomers were then polymerized using similar metal catalysts via a step-growth mechanism to result in the sequence-regulated vinyl copolymers in the main chain. Although the monomer sequencing in the main chain was perfectly controlled, the molecular weight was limited to the scale of thousands owing to the step-growth radical addition mechanism.

We herein conducted similar iterative ATRAs for styrene (S) and methyl acrylate (A) to synthesize a complete set of maleimide (M)-ended perfectly sequence-regulated “oligomonomers” consisting of trimeric vinyl monomer units (SSS, ASS, SAA, AAS, SSA, ASA, SAA, AAA) as substituents for the maleimide derivatives by further evolving the method we reported previously (Scheme 1).^{73,74} To see the effects of monomer sequences, the maleimide-ended oligomonomers were then radically homopolymerized or copolymerized with styrene (S)⁷⁵ or limonene (L)^{22–25} to produce high-molecular-weight vinyl copolymers comprising M, MS, or MML monomer sequences in the main chain in high yield. The obtained vinyl

copolymers should have a perfect trimeric sequence in the short side chains and 1:0, 1:1, or 2:1 monomer sequences in the long main chains. This would clarify the effects of monomer sequences on the properties of sequence-regulated vinyl copolymers.

RESULTS AND DISCUSSION

Maleimide-Ended Sequence-Regulated Oligomonomers by Iterative ATRAs. *Monomer Sequencing in the Side Chain.* A series of the maleimide-ended sequence-regulated oligomonomers were prepared via the ruthenium- or copper-catalyzed ATRAs of vinyl monomers, i.e., styrene (S) and methyl acrylate (A), to alkyl halides possessing monomeric S or A units iteratively (Scheme 2). We first conducted ATRA between S or A and the corresponding monomeric halide X-S (1-bromoethylbenzene or 1-chloroethylbenzene) or X-A (methyl 2-bromopropionate or methyl 2-chloropropionate) in excess of the halides (2–5 mol equiv to vinyl monomer) using appropriate ruthenium or copper complexes depending on the monomers and halides. The metal catalysts were chosen from those that especially give well-controlled molecular weights and narrow molecular weight distributions (MWDs) in the ATRP of the corresponding vinyl monomer with the halide initiators. This is because the catalyst that enables highly controlled molecular weights possesses a high ability to induce fast deactivation of the resulting radical species into the halide and is expected to provide the dimer in high yield by suppressing further polymerization as side reactions. According to the previous reports on the ATRPs, $\text{RuCp}^*\text{Cl}(\text{PPh}_3)_2$ was selected for activation of styrene-terminal halide while $\text{CuBr}/\text{PMDETA}$ or $\text{RuCp}^*\text{Cl}(\text{PPh}_3)_2$ was used for acrylate terminal halide.^{76,77} One of the notable features of ATRAs for the iterative radical addition reactions is that the chlorides and bromides are generally stable under air and can be purified by column chromatography or distillation. However, for preparation of the dimer with styryl terminal halide (Cl-SS or Cl-SA), the chloride (Cl-S or Cl-A) was used because the bromide terminal of the styrene proved to be less stable at high temperatures for the distillation.

Although the yields depended on the monomers, halides, and metal catalysts, all of these reactions resulted in the corresponding 1:1 adducts, i.e., dimers (X-SS, X-AS, X-SA, X-AA), which were purified by distillation or column chromatography. All of these four dimers were then iteratively reacted with S or A again in the presence of the appropriate metal catalysts to afford a complete set of the eight halogen-ended trimers (X-SSS, X-ASS, X-SAS, X-AAS, X-SSA, X-ASA, X-SAA, X-AAA).

In these iterative reactions, the yields for addition reactions between the acrylate halide terminal (X-A, X-AS, X-AA) and styrene or acrylate monomer were generally high (=70–90%) owing to the high reactivity of the acrylate halide terminal. In contrast, the addition reactions between the styrene halide terminal and styrene or acrylate resulted in lower yields. The yields between the styrene halide (X-S, X-SS, X-SA) and styrene were approximately 20–40% owing to the low reactivities of styrene halide,⁷⁸ which also resulted in a low conversion of styrene. Those between styrene halide (X-S, X-SS, X-SA) and acrylate were approximately 15–20%, where acrylate oligomers were formed owing to the higher reactivity of the resulting acrylate halide terminal than that of the starting styrene halide terminal.

The maleimide (M) group was introduced by an $\text{S}_{\text{N}}2$ reaction with furan-masked potassium maleimide anion and the halides followed by a retro Diels–Alder reaction for the deprotection of the furan group to yield the complete set of maleimide-ended perfectly sequence-regulated vinyl oligomonomers consisting of S and/or A trimeric units (M-SSS, M-ASS, M-SAS, M-AAS, M-SSA, M-ASA, M-SAA, M-AAA) with different monomer compositions or sequences, although they were each mixtures of diastereomers and enantiomers (Figure 1 and Figure S1). In addition, MALDI-TOF-MS analyses showed the formation of single molecular weight

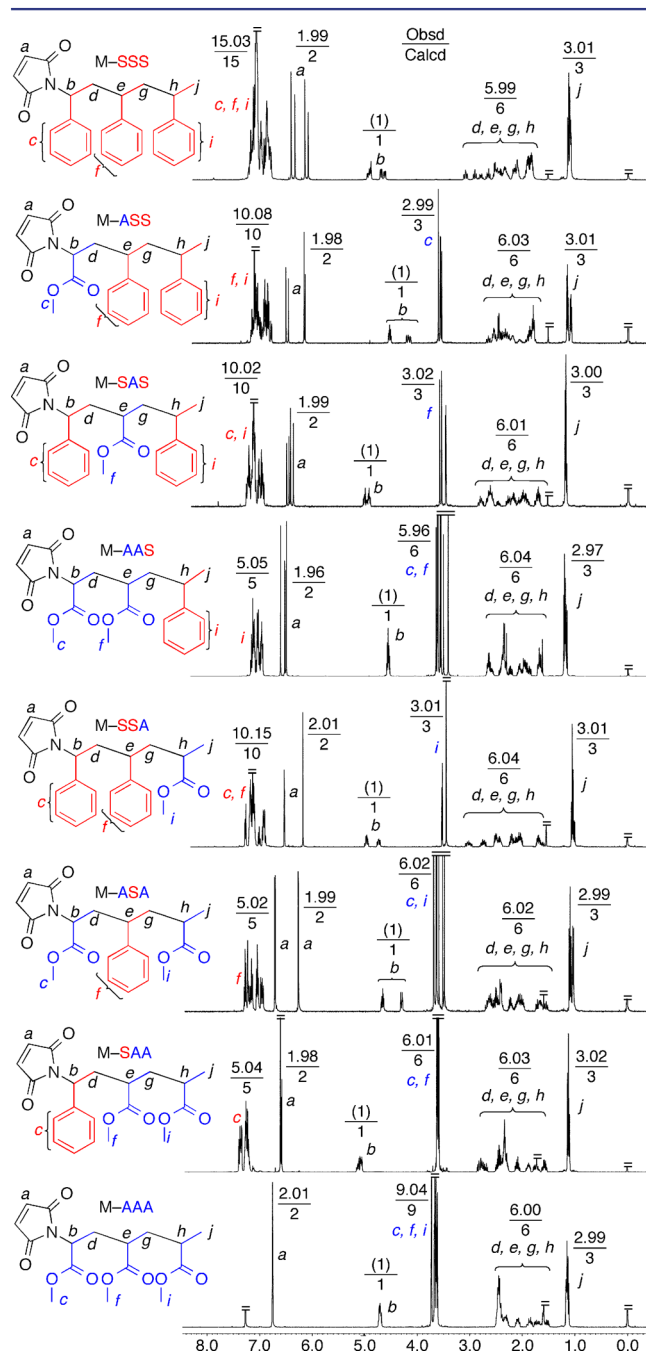


Figure 1. ^1H NMR spectra (CDCl_3 ; rt, room temperature) of a series of maleimide-ended sequence-regulated oligomonomers (M-SSS, M-ASS, M-SAS, M-AAS, M-SSA, M-ASA, M-SAA, M-AAA).

Table 1. 1:1 Alternating Free Radical Copolymerization of Maleimide-Ended Oligomonomer (M_1) and Styrene (S)^a

M_1	time (h)	conv ^b (%) M_1/S	M_n^c	M_w/M_n^c	incorp ^b (%) M_1/S	T_g^d (°C)	T_{ds}^e (°C)	cloud point ^f (°C) (THF/MCH)	cloud point ^f (°C) (THF/MeOH)
M-SSS	5	92/91	102 000	3.13	49/51	138	380		
M-ASS	7	94/94	181 000	3.76	50/50	131	370	21.4 (35/65)	34.0 (50/50)
M-SAS	7	93/94	125 000	3.75	49/51	112	370	20.6 (35/65)	10.8 (50/50)
M-AAS	7	96/98	176 000	3.29	50/50	100	360	soluble (50/50)	27.8 (45/55)
M-SSA	7	97/97	150 000	3.72	49/51	130	377	49.2 (35/65)	3.3 (50/50)
M-ASA	8	95/93	172 000	3.20	49/51	121	372	20.5 (50/50)	23.0 (45/55)
M-SAA	4	95/98	258 000	2.84	49/51	102	365	26.9 (50/50)	22.7 (45/55)
M-AAA	5	89/90	183 000	2.93	50/50	92	357		

^aPolymerization condition: $[M_1]_0 = [S]_0 = 1.0$ M, $[AIBN]_0 = 20$ mM, toluene, 60 °C. ^bDetermined by ¹H NMR. ^cDetermined by SEC. ^dObtained by differential scanning calorimetry. ^eDetermined by thermogravimetric analysis. ^fDetermined by transmittance measurement: 10 mg/mL solution; cooling rate = 1 °C/min; wavelength 500 nm.

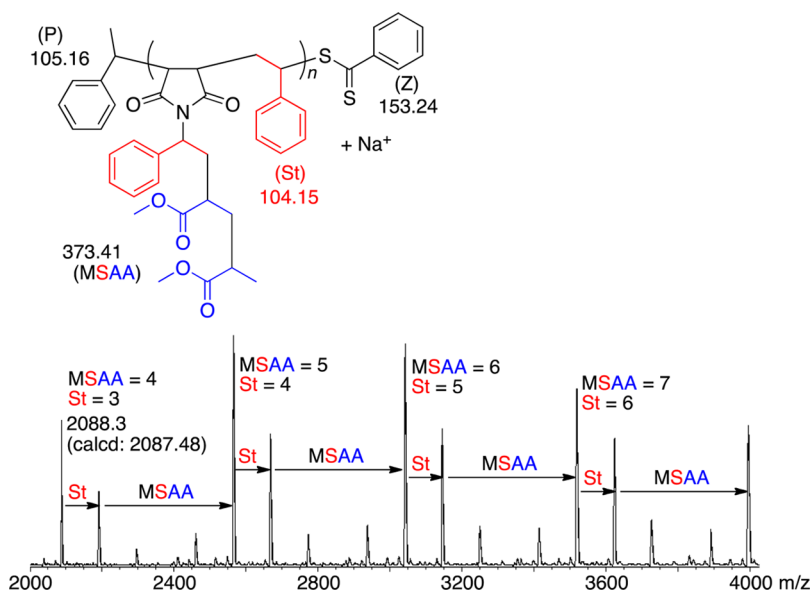


Figure 2. MALDI-TOF-MS spectrum (linear mode) of poly(M-SAA-*alt*-S) obtained in the RAFT copolymerizations ($[M_1]_0/[S]_0/[AIBN]_0/[PEDB]_0 = 1000/1000/5.0/20$ mM, 20% for M-SAA and 21% for styrene, $M_n = 3900$, $M_w/M_n = 1.33$).

compounds (Figure S2). These results indicate that the synthesis of perfectly sequence-regulated vinyl oligomers is possible in 5–10 g scales using appropriate metal catalysts and halides under optimized conditions in iterative ATRAs, although this has been considered to be almost impossible owing to the concurrently occurring ATRPs. However, there might be a practical limitation for the synthesis of higher oligomers based on this approach.

1:1 Alternating Radical Copolymerization of Maleimide-Ended Oligomonomers and Styrene. AB Monomer Sequencing in the Main Chain. The series of maleimide-ended sequence-regulated oligomonomers was then radically copolymerized with styrene at the 1:1 feed ratio with AIBN as the initiator in toluene at 60 °C. In all cases, both of the oligomonomers and styrene were consumed at the same rate almost quantitatively for 10 h to yield the copolymers with considerably high molecular weights ($M_n > 100\,000$) (Table 1, Figure S3).

The obtained copolymers were then analyzed by ¹H NMR. Similar but slightly different spectra were obtained for the polymers because of the presence of styrene and maleimide and/or acrylate units as their components and slight differences in the monomer compositions and sequences in the obtained vinyl copolymers (Figure S4). The incorporated ratios of the

maleimide-ended oligomonomers and styrene were thus measured by the peak intensity ratios in the ¹H NMR spectra, and all proved to be nearly 50/50 irrespective of differences in the trimeric monomer units in the side chains.

In addition, the reversible addition–fragmentation chain transfer (RAFT) copolymerization of the maleimide-ended oligomonomers and styrene was investigated using 1-phenylethylthiobenzoate (PEDB: PhEtSC(S)Ph) as a RAFT agent in the presence of AIBN at 60 °C to investigate the controllability of the molecular weight and chain-end groups of the resulting copolymers and clarify the monomer sequences in the main chain. The RAFT copolymerization proceeded at the same consumption rate of the maleimide-ended oligomonomer (M-SAA) and styrene (Figure S5) as in the free radical copolymerization. The resulting copolymers exhibited narrow MWDs ($M_w/M_n \sim 1.2$) and controlled molecular weights that increased in direct proportion to monomer conversion. The slightly lower molecular weights than the calculated values can be attributed to the lower estimation of the hydrodynamic volume of the resulting copolymers with pendent trimeric monomer units than that of standard polystyrene. The matrix-assisted laser desorption–ionization time-of-flight mass spectroscopy (MALDI-TOF-MS) revealed that the resulting copolymers possess the well-defined RAFT chain end-groups

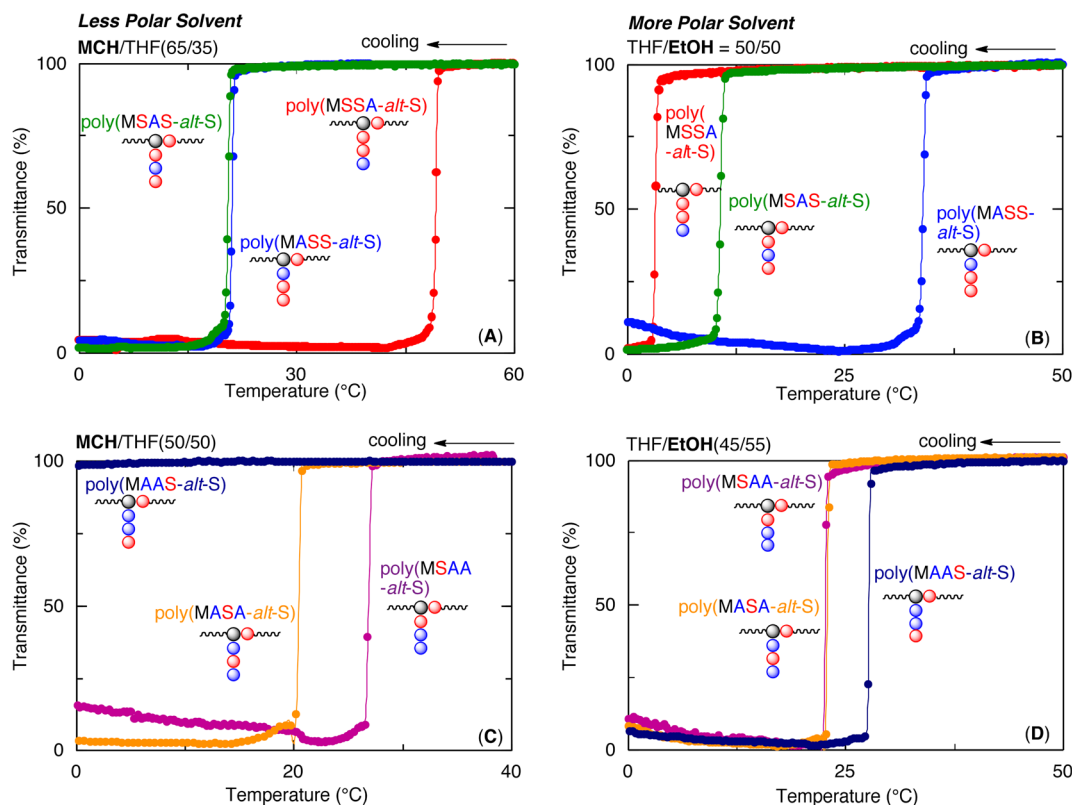


Figure 3. Transmittance of a series of main- and side-chain sequence-regulated vinyl copolymers [poly(M_1 -alt-S)] obtained in 1:1 alternating free radical copolymerization of maleimide-ended oligomonomers (M_1) and styrene at varying temperatures in (A) methylcyclohexane/THF (65/35) (M_1 : M-SSA, M-SAS, M-ASS), (B) THF/EtOH (50/50) (M_1 : M-SSA, M-SAS, M-ASS), (C) MCH/THF (50/50) (M_1 : M-SAA, M-ASA, M-AAS), and (D) THF/EtOH (45/55) (M_1 : M-SAA, M-ASA, M-AAS): 10 mg/mL; cooling rate = 1 °C/min; wavelength = 500 nm.

and alternating sequences comprising nearly the same numbers of each unit [$(n, m) = (k, k - 1), (k, k), (k, k + 1)$], where n and m represent the unit number of M-SAA and styrene in the main chain, respectively, with small exceptions [$(n, m) = (k, k - 2)$] (Figure 2). The most major series are those of $(n, m) = (k, k - 1)$, and the second most major are $(n, m) = (k, k)$, indicating that the RAFT copolymerization was most preferentially started from the addition of 1-phenylethyl fragment radical, i.e., unimer styryl radical, to M-SAA, and was predominantly terminated by the capping of dithiobenzoate to the M-SAA terminal.

All of these results indicate that the radical copolymerization of maleimide-ended oligomonomers and styrene proceeded in a highly alternating fashion to result in the AB monomer sequences in the main chain of the resulting vinyl copolymers, which also have perfectly sequence-regulated trimeric vinyl monomer units in the side chains.

Effects of Side-Chain Monomer Sequences on Polymer Properties. The effects of side-chain monomer sequences on the polymer properties were first investigated in terms of solubility of the polymers. The solubility was evaluated in two solvent mixtures with different polarity, i.e., methylcyclohexane (MCH)/THF as less polar solvents and THF/EtOH as more polar solvents, at varying temperatures by measuring the light transmittance of the polymer solutions at 500 nm (Figure 3).

To see the main effects of monomer sequences, the solubility was compared for a series of the copolymers with the same monomer composition but different monomer sequences. These series of copolymers can be regarded as a kind of

structural isomers of the copolymers. When a series of copolymers containing two styrene and one acrylate units, i.e., poly(M-ASS-alt-S), poly(M-SAS-alt-S), and poly(M-SSA-alt-S), was dissolved in MCH/THF (65/35) with a lower polarity, poly(M-SSA-alt-S) with acrylate in the outer unit was less soluble than the others: it became turbid at approximately 50 °C ($T_c = 49.2$ °C, T_c : cloud point), whereas the others did so at a lower temperature, approximately 20 °C (Figure 3A). In contrast, in THF/EtOH (50/50) with a higher polarity, the solubility of the copolymers increased as the acrylate unit came out from the inner to the outer of the monomer sequences in the side chains ($T_c = 34.0, 10.8$, and 3.3 °C for M-ASS, M-SAS, and M-SSA sequences, respectively) (Figure 3B). This indicates that monomer sequences in the side chains indeed affect the solubility and that the outer segments have more important roles for determining the solubility of the vinyl copolymers.

Another series of the isomeric copolymers that contain one styrene and two acrylate units, i.e., poly(M-AAS-alt-S), poly(M-ASA-alt-S), and poly(M-SAA-alt-S), was generally more soluble in polar solvents than the former series because it contains a higher amount of acrylate units. Regarding the effects of monomer sequences in this series on the solubility, similar tendencies were observed. As the hydrophobic styrene unit went in from the outside to the inside of the monomer sequences, the solubility in a less polar solvent, MCH/THF (50/50), decreased (Figure 3C). In contrast, in THF/EtOH (45/55) with a higher polarity, poly(M-AAS-alt-S) with styrene in the outer unit became turbid at higher temperature ($T_c = 27.8$ °C) than the others ($T_c = 23.0$ and 22.7 °C for M-

ASA and M-SAA, respectively) (Figure 3D). These results again indicate that not only the monomer compositions but also the monomer sequences are crucial for determining the solubility of the vinyl copolymers and that the solubility can be gradually changed by the monomer sequences in the side chains.

The effects of monomer compositions and sequences on the thermal properties of the sequence-regulated vinyl copolymers were then evaluated by differential scanning calorimetry (DSC). All copolymers are amorphous and exhibit glass transition temperatures (T_g 's) between 90 and 140 °C, which were dependent on both the monomer compositions and sequences (Figure 4). The highest T_g was observed for the copolymers of

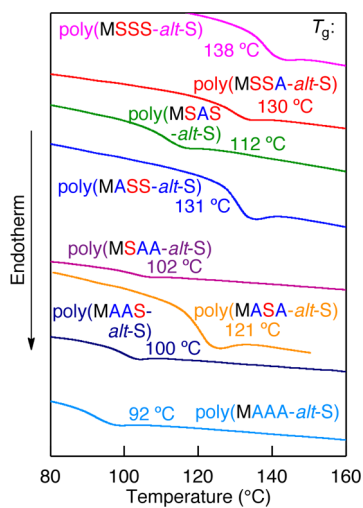


Figure 4. DSC curves and T_g values of a series of main- and side-chain sequence-regulated vinyl copolymers obtained in 1:1 alternating free radical copolymerization of maleimide-ended oligomonomers (M_1) and styrene [poly(M_1 -alt-S)] (A).

the highest styrene composition ($T_g = 138$ °C, poly(M-SSS-alt-S)), whereas the lowest T_g was found for the highest acrylate composition ($T_g = 92$ °C, poly(M-AAA-alt-S)). This demonstrates that the difference in monomer compositions in the side chains of the same main-chain alternating maleimide and styrene units can alter the T_g values in relatively wide ranges (~ 50 °C), in which the order is the same as that for the homopolymers of styrene ($T_g = 100$ °C) and methyl acrylate ($T_g = 10$ °C).

The effects of side-chain monomer sequences on T_g values were indeed observed for both series of isomeric copolymers. In the first series of isomeric copolymers with two styrene and one

acrylate units, the T_g values for the copolymers possessing two sequential styrene units, i.e., poly(M-SSA-alt-S) and poly(M-ASS-alt-S), were almost the same at approximately 130 °C, whereas that without sequential styrene units, i.e., poly(M-SAS-alt-S), exhibited a lower T_g at 112 °C. Similarly, in the second series of isomeric copolymers with one styrene and two acrylate units, the copolymers possessing two consecutive acrylate units, i.e., poly(M-SAA-alt-S) and poly(M-AAS-alt-S), exhibited nearly the same T_g values of approximately 100 °C, whereas the T_g of the copolymers without successive acrylate units, i.e., poly(M-ASA-alt-S), was higher (121 °C) than those of the two isomers. As we previously reported, for the copolymers consisting of the sequence-regulated dimeric units, no such effects of the monomer sequences on T_g values were observed.⁷⁴ These results indicate that the presence of two successive styrene (SS) units in the side chains is crucial for yielding relatively high T_g values of approximately 130 °C. A similar conclusion concerning two sequential acrylate (AA) units for relatively low T_g values of approximately 100 °C can also be derived. In addition, it is interesting to note that poly(M-ASA-alt-S) has a higher T_g than poly(M-SAS-alt-S) (121 °C vs 112 °C) irrespective of the lower styrene contents in the side chains. Thus, the monomer sequences even in the side chains can affect the thermal properties of vinyl copolymers.

The degradation temperatures (T_{d5} ; temperature at 5% weight loss) of these copolymers were also measured (Figure S6). All copolymers possessed similar T_{d5} values between 360 and 380 °C and showed relatively high thermal stability mainly originating from the main-chain alternating maleimide and styrene sequences. There were very few specific dependences of thermal decompositions on the monomer sequences.

2:1-Sequenced Radical Copolymerization of Maleimide-Ended Oligomonomers and Limonene. *AAB Monomer Sequencing in the Main Chain.* To control the monomer sequences in the main chain in a higher order, a series of the maleimide-ended sequence-regulated oligomonomers were copolymerized with limonene (L) at a feed ratio of 2:1 ($[\text{oligomonomer}]_0/[\text{L}]_0 = 2/1$) using V-70 as the initiator in $\text{PhC}(\text{CF}_3)_2\text{OH}$ at 20 °C.^{22–25} In all cases, oligomonomers and limonene were consumed at the same rate irrespective of the differences in the side-chain monomer compositions and sequences of the oligomonomers (Figure S7) to yield products of their molecular weights of approximately 10 000–20 000 based on the polystyrene standard calibration by SEC (Table 2). ¹H NMR analysis of the products shows that the products are vinyl copolymers between the maleimide-ended oligomonomers and limonene and that the incorporated oligomono-

Table 2. 2:1 Alternating Free Radical Copolymerization of Maleimide-Ended Oligomonomer (M_1) and Limonene (L)^a

M_1	time (h)	conv ^b (%) M_1/L	M_n ^c	M_w/M_n ^c	incorp ^b (%) M_1/L	T_g ^d (°C)	T_{d5} ^e (°C)
M-SSS	360	58/57	8300	1.69	66/34	138	336
M-ASS	480	55/52	8000	1.53	65/35	126	327
M-SAS	240	76/74	19 000	1.76	66/34	112	315
M-AAS	480	61/61	20 900	1.83	65/35	101	326
M-SSA	480	61/61	11 500	1.65	67/33	129	325
M-ASA	480	56/55	19 000	1.81	65/35	113	325
M-SAA	216	78/78	22 700	1.88	67/33	104	322
M-AAA	240	63/62	24 900	1.64	64/36	97	325

^aPolymerization condition: $[\text{M}_1]_0 = 800$ mM, $[\text{L}]_0 = 400$ mM, $[\text{V-70}]_0 = 8.0$ mM, $\text{PhC}(\text{CF}_3)_2\text{OH}$, 20 °C. ^bDetermined by ¹H NMR. ^cDetermined by SEC. ^dObtained by differential scanning calorimetry. ^eDetermined by thermogravimetric analysis.

monomers ratios are invariably 64–67%, independent of the side-chain compositions and sequences and are nearly the same as the value 2/3, assuming that the ideal 2:1 copolymerization proceeds (Figure S8).

To clarify the monomer sequences in the main chain of the copolymers, the RAFT copolymerization of one of the maleimide-ended oligomonomers (M–SAA) and limonene was conducted at the 2:1 feed ratio using S-cumyl S'-butyl trithiocarbonate (CBTC: CumSC(S)Bu) as the RAFT agent and AIBN as the initiator in PhC(CF₃)₂OH at 60 °C. Both monomers were consumed at the same rate as in the free radical copolymerization without RAFT agents (Figure S9). The molecular weights of the copolymers increased with monomer conversion but were lower than the calculated values. One of the main reasons for the lower molecular weights is the difference in the hydrodynamic volumes of standard polystyrene, as suggested by the fact that the absolute molecular weight measured by multiangle light scattering (MALLS) equipped with the SEC was close to the calculated value ($M_n(\text{MALLS}) = 10\,800$, $M_n(\text{calcd}) = 9400$). The controlled terminal structures with RAFT end-groups and the AAB sequence-regulated main-chain structures were confirmed by the MALDI-TOF-MS spectrum (Figure 5). The molar masses

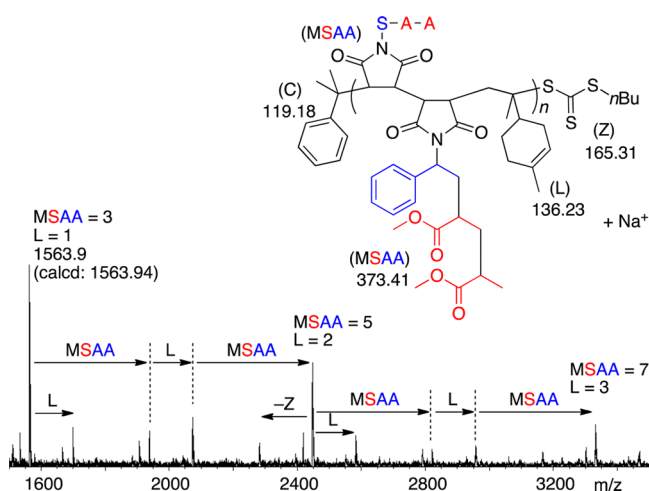


Figure 5. MALDI-TOF-MS spectrum (linear mode) of poly(M–SAA-co-Lim) obtained in the RAFT copolymerizations ($[\text{M}_1]_0/[\text{Lim}]_0/[\text{AIBN}]_0/[\text{CBTC}]_0 = 800/400/5.0/12$ mM, 8% for M–SAA, and 8% for limonene, $M_n = 1800$, $M_w/M_n = 1.41$).

of the main series of peaks were separated by the same intervals (883.05) as those for AAB (A, M–SAA; B, limonene) monomer sequences and were very close to those calculated for the copolymers consisting of (Cum-(AAB)_n-A-SC(S)-Bu).^{22–25} These results indicate that the 2:1 sequenced radical copolymerization proceeded similarly, even for the maleimide-ended oligomonomers and limonene in the fluorinated alcohol to give the AAB monomer sequences in the main chain.

DSC was also conducted for the series of main-chain AAB-sequenced vinyl copolymers of maleimide-ended sequence-regulated oligomonomers and limonene (Figure 6). The effects of side-chain monomer components and sequences on T_g values of the copolymers were quite similar to those observed for the series of main-chain AB-sequenced vinyl copolymers of oligomonomers and styrene. The T_g values were varied between 138 °C for the copolymers of the highest styrene composition and 97 °C for the highest acrylate composition.

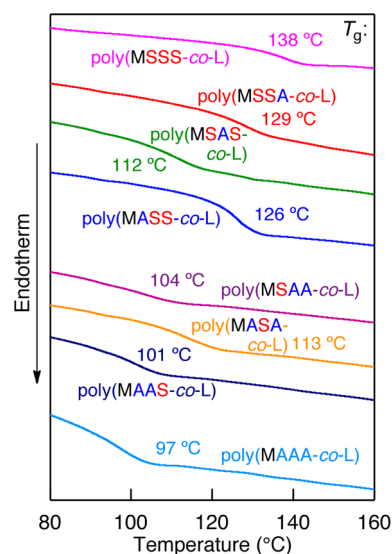


Figure 6. DSC curves and T_g values of a series of main- and side-chain sequence-regulated vinyl copolymers obtained in 2:1 alternating radical copolymerization of maleimide-ended oligomonomers (M_1) and limonene [$\text{poly}(\text{M}_1\text{-co-Lim})$].

Interestingly, these T_g values (138 and 97 °C) were nearly the same as those of the above-mentioned main-chain AB-sequenced alternating vinyl copolymers (138 and 92 °C) irrespective of the differences in the main-chain components and sequences, i.e., MML and MS.

With regard to the effects of side-chain sequences, the copolymer with alternating SAS sequences in the side chain has a lower T_g (112 °C) than that with SSA (129 °C) or ASS (126 °C), in which both the latter copolymers with a homo-SS side-chain sequence exhibited similarly higher T_g values of approximately 125–130 °C. These values of the main-chain AAB-sequenced copolymers with two styrene and one acrylate units in the side chains are almost the same as those of the main-chain AB-sequenced copolymers with the same monomer sequences as mentioned above. For another series of isomeric main-chain AAB-sequenced vinyl copolymers, the copolymer with alternating ASA sequence in the side chain has a higher T_g (113 °C) than that with SAA (104 °C) and AAS (101 °C), in which both copolymers with homo-AA side-chain sequence exhibited similarly lower T_g 's of approximately 100–105 °C. These values of the main-chain AAB-sequenced copolymers with one styrene and two acrylate units in the side chains are similar to those of the main-chain AB-sequenced copolymers with the same monomer sequences, although that with a side-chain ASA sequence was slightly lower for the main-chain AAB than AB (113 °C vs 121 °C). Such small dependences on the main-chain monomer sequences are most probably due to small differences in the structure of styrene and limonene, both of which possess pendent six-membered rings.

The degradation temperatures of the main-chain AAB-sequenced copolymers were between 315 and 336 °C (Figure S10) and were invariably lower than those of the main-chain AB-sequenced copolymers (360–380 °C). The lower thermal stability of the main-chain AAB-sequenced copolymer can be attributed to several factors such as the presence of a remaining C=C double bond in the limonene unit, a main-chain quaternary carbon originating from the vinylidene structure of limonene, and a bulky maleimide-maleimide sequence in the main chain.

Table 3. Free Radical Homopolymerization of Maleimide-Ended Oligomonomer (M_1)^a

M_1	time (h)	conv ^b (%)	M_1	M_n^c	M_w/M_n^c	M_n^d	T_g^e (°C)	T_g^∞ (°C)	T_{d5}^g (°C)
M-SSS	180	92		3000	1.31	6300	122		354
M-ASS	24	95		8300	2.19	15 600	131	138	354
M-SAS	36	96		9500	1.66	17 700	103	106	342
M-AAS	20	95		16 900	1.72	36 300	77	82	342
M-SSA	120	94		7900	1.36	13 400	129	142	348
M-ASA	25	95		17 200	1.69	29 400	130	132	372
M-SAA	30	92		16 100	1.40	31 700	122	140	340
M-AAA	7	95		11 500	2.47	24 900	53		335

^aPolymerization condition: $[M_1]_0 = 1.0$ M, $[AIBN]_0 = 10$ mM, toluene, 60 °C. ^bDetermined by ¹H NMR. ^cDetermined by SEC. ^dDetermined by MALLS. ^eDetermined by DSC. ^fDetermined by Flory–Fox equation. ^gDetermined by thermogravimetric analysis.

Radical Homopolymerization of Maleimide-Ended Oligomonomers. Homosequencing in the Main Chain. In general, maleimides can also be radically homopolymerized, although the rate for homopropagation is smaller than that for the alternating copolymerization with styrene. To see the effects of the side-chain monomer sequences on the homopolymers and differences among the main-chain A-homo, AB-alternating, and AAB-monomer sequences, a series of maleimide-ended oligomonomers were homopolymerized in toluene at 60 °C using AIBN as the initiator.

In all cases, the homopolymerizations occurred quantitatively (Figure S11) although the rates were smaller than those of the alternating copolymerization with styrene, which were completed in 10 h under similar conditions (Figure S3). It is interesting to note that the homopolymerization was fastest for the maleimide-ended oligomonomer with the side-chain AAA sequence and slowest for the SSS sequence. In addition, the rate decreased as the side-chain styrene unit came into the inner sequence or the number of the styrene unit increased. Thus, the order of the rate is as follows: M-AAA > M-AAS > M-ASA > M-SAA ~ M-ASS > M-SAS > M-SSA > M-SSS. This could be related to the bulkiness of the side-chain groups near the maleimide groups because the styrene unit is bulkier than methyl acrylate. In homopolymerization of the maleimide-ended oligomonomers, the steric hindrance around the propagating maleimide radical species is more crucial than the copolymerization, in which the steric hindrance between the propagating chain and the incoming monomer can be eased by the relatively small comonomer such as styrene.

As shown in Table 3, such differences in the polymerization rate originating from the side-chain sequences affect the molecular weights of the resulting homopolymers. The molecular weights were lowest (M_n (SEC) = 3000 based on polystyrene calibration, M_n (MALLS) = 6300) for poly(M-SSS) obtained in the slowest polymerization and were still lower (M_n (SEC) = 8000–10000, M_n (MALLS) = 13 000–18 000) for the polymers containing two styrene units in the side chains. The polymers that contain two or three acrylate units in the side chains had invariably higher molecular weights (M_n (SEC) = 10 000–20 000, M_n (MALLS) = 25 000–36 000). ¹H NMR analysis also showed that the obtained products were homopolymers of the maleimide-ended oligomonomers via polymerization of the maleimide moiety (Figure S12).

Finally, the thermal properties of the homopolymers with different side-chain monomer compositions and sequences were evaluated by DSC and TGA. The T_g values were highest (122 °C) again for the homopolymers consisting of SSS side-chain sequences and lowest (53 °C) for AAA sequences irrespective of the lower molecular weights for poly(M-SSS).

Both of these values were lower than those of the main-chain AB-alternating or AAB-monomer-sequenced polymers. This might be ascribed to lower molecular weights of the obtained homopolymers but are based on SEC.

To exclude the effects of molecular weights and compare only the effects of side-chain monomer compositions and sequences on T_g values, the resulting polymers were then fractionated by preparative SEC and subjected to the DSC measurement because there were relatively large differences in molecular weights of the resulting homopolymers depending on the side chains. The T_g values were measured for each fraction and plotted against the reciprocal M_n of each fraction to estimate the T_g for an infinite molecular weight, i.e., T_g^∞ , using the Flory–Fox equation (Figure S13). Among a series of isomeric homopolymers of the maleimide-ended oligomonomers possessing two styrene and one acrylate units, those with SS sequences show higher T_g^∞ 's (142 °C for poly(M-SSA) and 138 °C for poly(M-ASS)) than those of the alternating SAS sequence ($T_g^\infty = 106$ °C) in a similar way to the same series of isomeric main-chain AB-alternating or AAB-sequenced copolymers. Regardless of homopolymers of maleimide derivatives, which are expected to have rigid main chains originating from the cyclic repeating units, the T_g values of the homopolymers are similar to those of the main-chain AB- and AAB-copolymers. With regard to another series of isomeric homopolymers with one styrene and two acrylate units in the side chains, T_g^∞ with the alternating ASA sequence was higher ($T_g^\infty = 140$ °C) than those with AA sequences ($T_g^\infty = 132$ °C for poly(M-SAA) and 82 °C for poly(M-AAS)) similar to those of the same series of main-chain AB- and ABB-sequenced copolymers. However, the T_g^∞ of poly(M-SAA) with side-chain AA sequences was closer to that of poly(M-ASA) than poly(M-AAS), suggesting that the homopolymer of M-SAA has a relatively high T_g , which is difficult to expect from other results. The decomposition temperatures of the homopolymers were varied from 335 to 372 °C and were roughly between those of the main-chain AAB- and AB-sequenced copolymers.

CONCLUSIONS

We succeeded in the synthesis of a complete set of maleimide-ended sequence-regulated oligomonomers consisting of trimeric vinyl monomer units of styrene and/or methyl acrylate via iterative ATRAs by choosing appropriate metal catalysts depending on the monomers and halide terminals in each step. The obtained maleimide-ended oligomonomers were radically copolymerized with styrene via alternating AB-fashion or with limonene via 2:1 AAB-fashion successfully to result in the high-molecular-weight vinyl copolymers with sequence-regulated structures in both main and side chains. The main- and side-

chain monomer compositions and sequences affected not only the solubility but also the thermal properties of the sequence-regulated vinyl copolymers. The outer monomer unit in the side chains is crucial for the solubility, whereas the consecutive monomer unit, i.e., homo- or alternating sequences, in the side chains is important for determining T_g . This study first demonstrated such dependences of polymer properties in vinyl copolymers, although monomer-sequence effects are well-known for natural polymers such as proteins and nucleic acids. This synthetic strategy can be applied to various vinyl monomers and will further contribute to the development of high-performance or functional polymeric materials based on the sequence-regulated vinyl copolymers.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b11631.

Experimental procedures and supplementary data (PDF)

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Notes

The authors declare no competing financial interest.

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