Construction of Sequence-Regulated Vinyl Copolymers via Iterative Single Vinyl Monomer Additions and Subsequent Metal-Catalyzed Step-Growth Radical Polymerization

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ABSTRACT: A series of sequence-regulated vinyl copolymers with high-order and long vinyl monomer sequences were constructed via a combination of iterative single vinyl monomer additions, which were mediated by radical and cationic intermediates, and subsequent metal-catalyzed step-growth radical polymerization. The construction of vinyl monomer sequences was attained by iterative single monomer radical and cationic additions between a dichloride, having a similar substituent to that of vinyl monomers, and vinyl monomers such as styrenes, acrylates, and acrylonitrile. The resulting products were converted into sequence-regulated ab-type monomers that have embedded vinyl monomer sequences between an unconjugated C=C bond and reactive C–Cl bond via selective allylation of one of the two C–Cl bonds at their terminals. The synthesized sequence-regulated ab-type monomers were polymerized via metal-catalyzed step-growth radical polymerization, which resulted in vinyl chloride units via repetitive intermolecular addition reactions between the C=C and C–Cl terminals. Alternatively, aa- and bb-type sequence-regulated monomers, which have two unconjugated C=C and two reactive C–Cl bonds, respectively, were prepared by similar iterative single monomer additions and were subsequently polymerized via metal-catalyzed step-growth radical polymerization. The repeating vinyl monomer sequence codes in the resulting polymers, such as ABCC, ABCD, ABBAC, ABDBAC, and ABDBACAEEAC, varied from 4 to 11 monomer units in which the embedded vinyl monomer units were styrenes, acrylates, acrylamides, acrylonitrile, vinyl chloride, vinylidene chloride, and ethylene.

INTRODUCTION

Vinyl polymers are a major class of commodity polymers, including polyethylene, polypropylene, polystyrene, poly(vinyl chloride), poly(vinylidene chloride), poly(methyl methacrylate), poly(acrylic acid), polyacrylamide, polyacrylonitrile, poly(vinyl acetate), etc. These polymers are prepared by chain-growth polymerization of vinyl ($CH_2=CHR^1$) and vinylidene ($CH_2=CR^1R^2$) compounds using appropriate active species, such as radical, anionic, cationic, and organometallic species, for the corresponding monomers.[1] These various vinyl polymers are essential in our modern life and are used as plastics, rubbers, and fibers and in many applications such as packaging, building, construction, automotive applications, electrical applications, electronics, and agriculture because their substituents (R^1 and R^2) greatly affect the polymer properties. Furthermore, many vinyl monomers can be copolymerized to result in copolymers whose properties can be varied, tuned, or improved by the comonomer components and compositions. Various vinyl copolymers have thus been commercialized and utilized in industry.

Monomer sequences are important primary structural parameters of natural macromolecules, such as peptides, proteins, and nucleic acids, as the monomer sequence dictates the higher-order structures and thereby endows the macromolecules with special functions.[2] In these natural macromolecules, the monomer sequences are perfectly controlled through biological synthetic processes governed by biocatalysts, such as enzymes and ribozymes. In contrast, in synthetic polymers, particularly in vinyl polymers, the control of monomer sequences has long been one of the most challenging topics.[3–10] Radical copolymerization is one of the most efficient methods for making vinyl copolymers due to the high reactivity of propagating radical species toward a wide range of vinyl monomers, whereas the monomer sequences in the resulting copolymers are statistically distributed and governed by the reactivity ratio of the monomers.[11] The recent progress in controlled/living polymerizations has enabled the synthesis of various multiblock copolymers, in which segmented monomer sequences are controlled by sequential additions of monomers during chain-growth polymerizations.[12–22]

However, the control of the monomer sequence at the single monomer unit level is difficult in chain-growth copolymerization, which generally results in statistical sequences with statistical distributions. In some extreme cases, alternating copolymers with AB monomer sequences, such as a styrene-maleic anhydride sequence, form due to selective cross-propagation reactions.[11] The predominant AB alternating cross-propagation between styrene (A) and maleimide (B) was utilized to place a nearly single maleimide monomer unit approximately at desired positions in polystyrene chains by addition of a slight excess of one equivalent of maleimide per chain during the controlled/living radical polymerization of styrene,[23,24] although a statistical distribution of maleimide

units in the chain was inevitable. In addition to 1:1 AB alternating monomer sequences,[25] higher-order arrangements, such as 1:2 ABB monomer sequences, have been attained using strong penultimate effects for certain pairs of monomers, such as limonene (A) and maleimides (B), during radical copolymerization in fluorinated alcohols.[26–30] However, even in these selective AB or ABB alternating copolymerizations, the monomer sequence control is not perfect because the sequences are statistically governed by chain propagation. In addition, further longer and/or more complicated monomer sequences are essentially impossible in the chain-growth copolymerization of vinyl monomers.
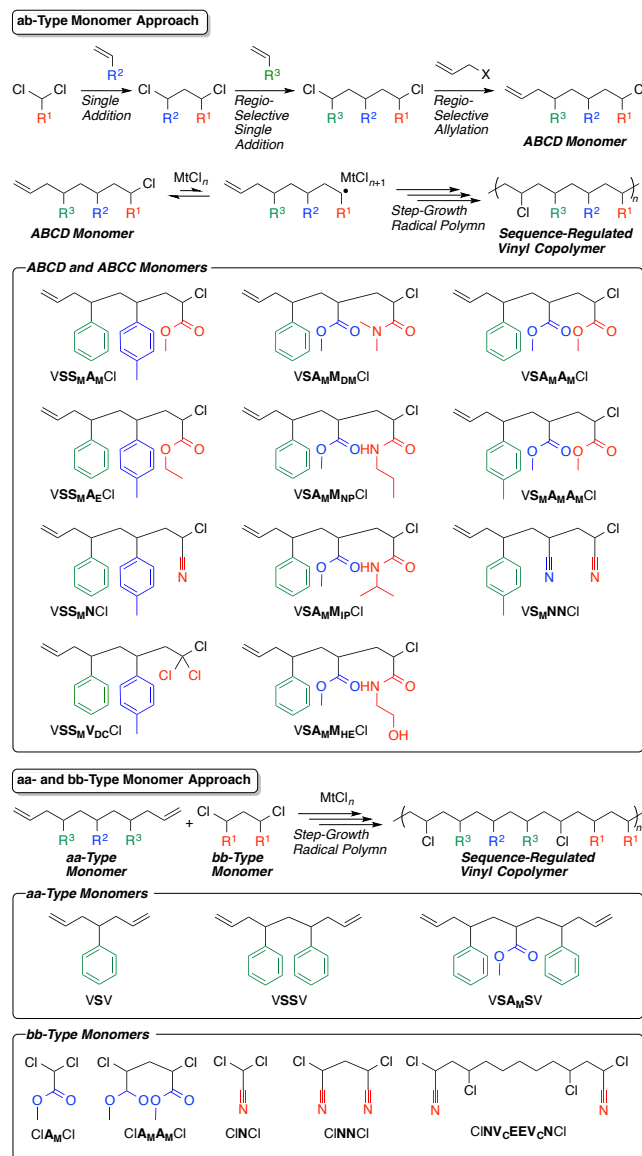
Although there have been several approaches using templates and neighboring effects for chain-growth copolymerization of vinyl monomers, the sequence regulation is not still perfect or is limited to only low-molecular-weight oligomers.[31–37] Alternatively, iterative single unit monomer additions or insertions have been conducted using the same systems as those for controlled/living polymerizations, though such processes are essentially limited to low-molecular-weight oligomers consisting of several monomer units.[38–52] Another strategy is based on the synthesis of sequence-programmed monomers or oligomers embedded with vinyl monomer units followed by appropriate polymerizations into polymers.[53–63]

For constructing vinyl monomer sequences in polymer main chains, we have developed a novel metal-catalyzed step-growth radical polymerization that proceeds between an unconjugated C=C bond (a) and radical species generated from a reactive C–Cl bond (b) in the designed ab-type monomer ($CH_2=CH–R–Cl$) to give a polymer connected via the resulting $–CH_2–CH(Cl)–$ unit in the main chain.[64,65] Since the resulting unit can be regarded as an equivalent structure to a vinyl chloride monomer unit ($–CH_2–CH(Cl)–$), we have proposed a novel strategy for sequence-regulated vinyl copolymers utilizing this unit as one of the sequence-regulated vinyl monomer units in the main chain.[53] Namely, in our previous communication, we prepared a sequence-programmed monomer by iteratively performing metal-catalyzed atom transfer radical addition (ATRA) of acrylate and styrene to an appropriate dichloride followed by allylation of the styrene terminal carbon–chlorine bond; thus, sequence-regulated vinyl monomer units were constructed in the R group in the designed monomer, such as $CH_2=CH–CH_2CH(Ph)–CH_2CH(CO_2Me)–CH_2CH(CO_2Me)–Cl$, which was then polymerized via metal-catalyzed step-growth radical polymerization to result in a structure equivalent to that of sequence-regulated vinyl polymers consisting of vinyl chloride (A)-styrene (B)-methyl acrylate (C)-methyl acrylate (C) units, described as $(ABCC)_n$. However, there are limitations in the variety of vinyl monomers and the higher-order monomer sequences, long monomer units, and molecular weights of the resulting polymers. To establish this strategy, further challenges must be addressed in not only constructing sequence-regulated monomers from various vinyl monomers but also developing more effective metal-catalyzed step-growth radical polymerizations.

In this paper, we widened the scope of vinyl monomer units and variety of monomer sequences by further developing the synthetic methods for sequence-regulated monomers and designing step-growth radical polymerizations (Scheme 1). We thus extended the vinyl monomer units to *p*-methylstyrene, acrylonitrile, acrylamides, vinylidene chloride, and ethylene not only to increase variety but also to enable more efficient synthesis of sequence-regulated monomers and polymers. To construct higher-order monomer sequences such as an ABCD sequence in an ab-type monomer, we examined not only radical but also cationic single monomer additions and selective amidation of the terminal acrylate unit (C) in the ABCC tetramer. Furthermore, to make higher-order and longer monomer sequences, we synthesized aa- and bb-type monomers possessing two unconjugated C=C bonds and two reactive C–Cl bonds, respectively, via similar ATRAs of vinyl monomers and investigated the metal-catalyzed step-growth radical polymerizations between the aa- and bb-type monomers.

Scheme 1. A Series of Sequence-Regulated Monomers Prepared by Iterative Single Monomer Additions and Metal-Catalyzed Step-Growth Radical Polymerization for Sequence-Regulated Vinyl Copolymers
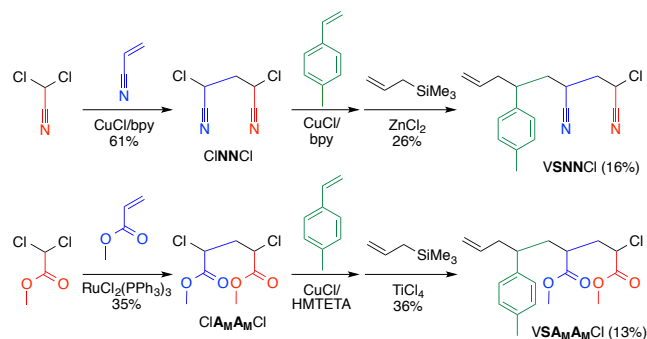

RESULTS AND DISCUSSION

Synthesis of ab-Type Monomers with ABCC and ABCD Vinyl Monomer Sequences. The previously reported synthetic method for the ABCC tetramer consists of a series of three consecutive reactions, i.e., a first ATRA of methyl acrylate (A_M) to methyl dichloroacetate (ClA_MCl) to produce the

CC dimer, a second ATRA of styrene (**S**) to either of the two carbon–chlorine bonds of the CC dimer to prepare the BCC trimer, and subsequent Lewis-acid catalyzed selective allylation of the resulting styryl carbon–chlorine bond in the BCC trimer to produce the ABCC tetramer.[53] The obtained products thus consist of vinyl (**V**), styrene, methyl acrylate, methyl acrylate, and chloride (**Cl**) sequences (VSA$_M$A$_M$Cl) though the ABCC tetramer is a mixture of diastereomers and enantiomers.

Here, we employed this approach for the synthesis of an acrylonitrile-containing ABCC tetramer (VS$_M$NNCl) (Scheme 2), in which the B and C units are *p*-methylstyrene (**S$_M$**) and acrylonitrile (**N**), respectively (Figure S1). The pure ABCC tetramer was obtained although the total isolation yield was moderate (16%). The reactions proceeded smoothly in comparison to the former acrylate-based tetramer due to several factors, i.e., the higher reactivity of the C–Cl bond adjacent to the acrylonitrile unit in the first and second steps,[66] more efficient reaction between electron-deficient acrylonitrile radical and the electron-rich C=C bond of *p*-methylstyrene in the second step, and higher reactivity of the C–Cl bond adjacent to the more electron-donating *p*-methylstyrene unit than that of styrene for the Lewis acid-catalyzed activation in the third step. In addition, an acrylate-based ABCC tetramer with methyl acrylate and *p*-methylstyrene units (VS$_M$A$_M$A$_M$Cl) was synthesized (Figure S2) to compare the reactivity of the acrylonitrile unit with that of acrylate in subsequent metal-catalyzed step-growth radical polymerization, as will be evaluated later.

Scheme 2. Synthesis of ab-Type Monomers with ABCC Sequence via Iterative ATRAs Followed by Selective Allylation
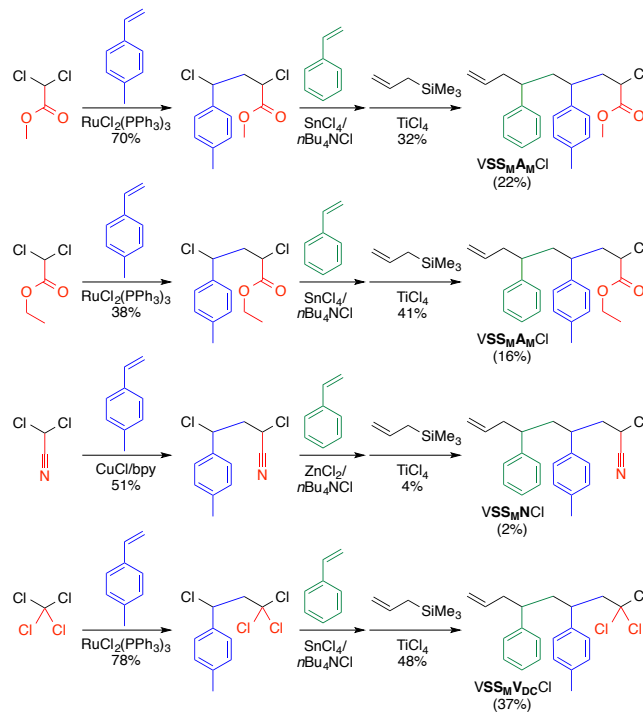

[a]The values in percentages below arrows and in parentheses indicate yields for each reaction and total yields of final products, respectively.

However, for construction of the ABCD sequence, this strategy based on iterative reactions only via radical intermediates seems unsuitable. The completely selective radical activation of either of the two carbon–chlorine bonds in the CD dimer is difficult and may result in a mixture of BCD and CDB trimers, as long as common vinyl monomers such as styrene and acrylate are used as C and D units. Another reasonable synthetic strategy should be developed for preparing an ABCD tetramer without contamination with different monomer sequences.

As the first strategy for the selective synthesis (Scheme 3), we examined cationic single monomer (B) addition via Lewis acid-catalyzed selective activation of the carbon–chlorine bond adjacent to the styrenic monomer (C) unit rather than that of the acrylic unit (D) in the CD dimer to exclusively synthesize the BCD trimer without any contamination of a CDB

sequence. We here used the system for living cationic polymerization of styrene derivatives.[67,68] To induce this process more efficiently, *p*-methylstyrene was selected as the C unit, whereas the D and B units were methyl acrylate and styrene, respectively. In this strategy, after the first ATRA of *p*-methylstyrene (C) to ClA$_M$Cl (D), the resulting *p*-methylstyryl carbon–chlorine bond in the CD dimer (ClS$_M$A$_M$Cl) is selectively activated by a Lewis acid to generate the relatively stable *p*-methylstyryl cation, which undergoes addition of styrene (B) to form the BCD trimer (ClSS$_M$A$_M$Cl) because the other C–Cl bond adjacent to acrylate in the CD dimer is inactive to Lewis acids.

Scheme 3. Synthesis of ab-Type Monomers with ABCD Sequence via Iterative Radical and Cationic Single Monomer Additions Followed by Selective Allylation

[a]The values in percentages below arrows and in parentheses indicate yields for each reaction and total yields of final products, respectively.

In addition, during cationic addition, unfavorable successive styrene polymerization can be diminished compared with the single monomer addition due to the higher reactivity of the original *p*-methylstyryl carbon–chlorine bond than that of the styryl bond in the resulting BCD trimer. This was indeed indicated by a preliminary result for the living cationic polymerization of styrene from the CD dimer under a large excess of styrene ([styrene]$_0$/[ClS$_M$A$_M$Cl]$_0$ = 500/25 mM) in the presence of SnCl$_4$ and *n*Bu$_4$NCl in CH$_2$Cl$_2$, where the CD dimer was consumed immediately to efficiently result in the BCD trimer rather than to form the polymer, especially at an early stage of the polymerization (Figure S6).

We then examined cationic single styrene addition to the CD dimer using the same catalyst with a slight excess of styrene with respect to the CD dimer ([styrene]$_0$/[CD dimer]$_0$ = 550/500 mM) and optimized the reaction conditions for selective trimer formation by mixing a nonpolar solvent, methylcyclohexane (MCHx), with CH$_2$Cl$_2$ to suppress styrene polymer-

ization (Figure S7). In CH_2Cl_2/MCHx (9/1 v/v), the single styrene addition proceeded smoothly and resulted in a higher content of the BCD trimer. Allylation followed without isolation of the trimer upon the addition of allyltrimethylsilane and $TiCl_4$ as a stronger Lewis acid catalyst to activate the resulting less reactive styryl C–Cl bond in the BCD trimer. The ABCD tetramer (VSS_MA_MCl) was formed and isolated by distillation in relatively good yield (37%) (Figure 1A).

We further synthesized a series of ABCD tetramers to extend the scope of this strategy. Namely, ethyl dichloroacetate (ClA_ECl), 2,2-dichloroacetonitrile (ClNCl), or carbon tetrachloride (CCl_4) was employed as the D unit in place of ClA_MCl in the first ATRA with p-methylstyrene as the C unit (Figures 1B–1D). For ClA_ECl and CCl_4, ruthenium catalyst $[RuCl_2(PPh_3)_3]$ was employed as for ClA_MCl,[69,70] whereas CuCl/2,2'-bipyridyl (bpy) was used for ClNCl because CuCl/bpy is effective for the atom transfer radical polymerization (ATRP) of acrylonitrile.[71,72] For the obtained CD dimers, the cationic single addition of styrene as the B unit was similarly conducted using $SnCl_4$ or $ZnCl_2$ as the Lewis acid catalyst in the presence of nBu_4NCl under optimized conditions. The obtained BCD trimers were subsequently allylated without isolation. In all cases, after distillation, pure ABCD tetramers were obtained. These ABCD tetramers, which were obtained from ClA_ECl, ClNCl, and CCl_4 possess ethyl acrylate (A_E), acrylonitrile (N), vinylidene chloride (V_{DC}) units as the D units, respectively, whereas the ABC units are the same (VSS_M). These ABCD tetramers can thus be denoted by VSS_MA_ECl, VSS_MNCl, and $VSS_MV_{DC}Cl$.

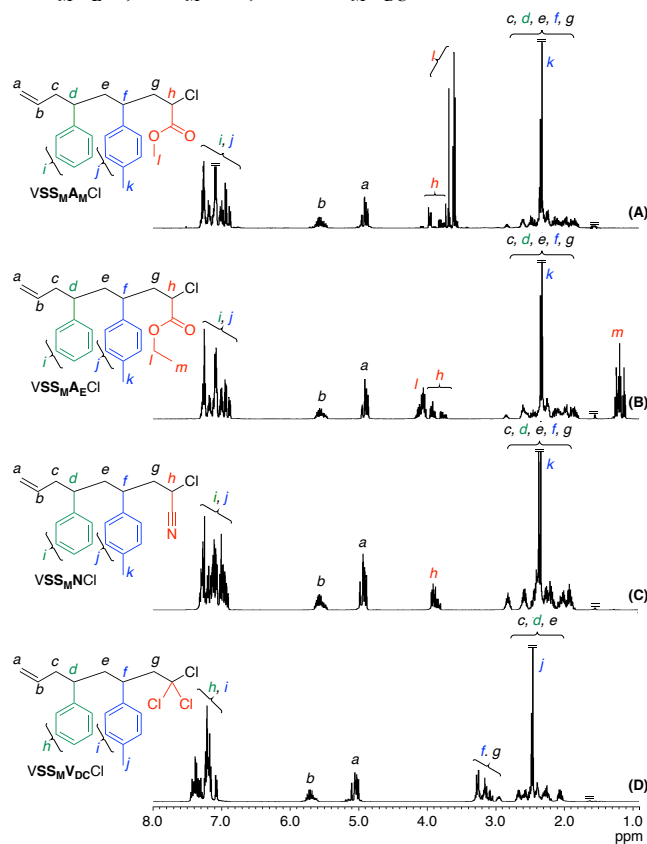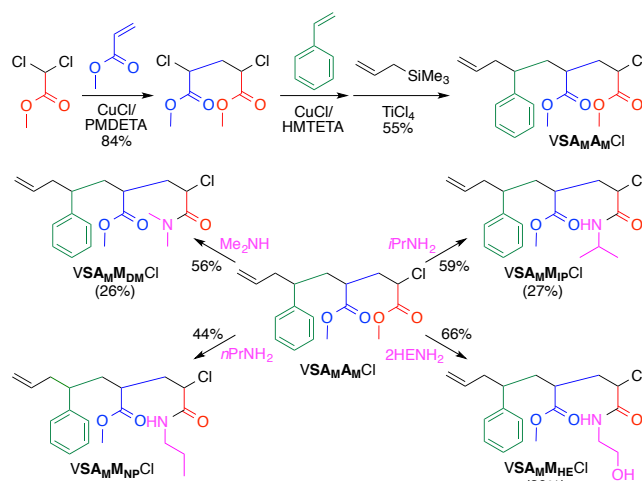**Figure 1.** ^1H NMR spectra (CDCl$_3$, 25 °C) of a series of ab-type sequence-regulated monomers with ABCD sequences: (A) VSS_MA_MCl, (B) VSS_MA_ECl, (C) VSS_MNCl, (D) $VSS_MV_{DC}Cl$.

As a second strategy for another series of ABCD tetramers, we found that selective amidation of the ester group (C) adjacent to the terminal carbon–chlorine bond in the ABCC tetramer (VSA_MA_MCl) occurred and was useful (Scheme 4). Although the carbon–halogen (C–X) bond generally undergoes an S_N2 reaction by primary and secondary amines (R^1R^2NH) to produce the corresponding alkyl amines (C–NR^1R^2), we found that α-chloroester (C(CO$_2$R)–Cl) undergoes selective amidation (C(CONR^{1}R^2)–Cl) of the ester moiety under optimized conditions instead of the S_N2 reaction.

Scheme 4. Synthesis of ab-Type Monomers with ABCD Sequence Containing Acrylamide Derivative Units via Selective Amidation of Terminal Acrylate Unit of ABCC Sequence in VSM$_A$M$_A$Cl

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

As model reactions, we mixed a halide comprising a methyl acrylate dimer [CH$_3$CH(CO$_2$Me)–CH$_2$CH(CO$_2$Me)–X (A_MA_MX); X = Cl, Br] and a large amount of dimethylamine without any catalysts (Figure S8). The bromide mainly underwent an S_N2 reaction and resulted in a dimethylamino-substituted dimer ($A_MA_MNMe_2$) along with an amidated byproduct [CH$_3$CH(CO$_2$Me)–CH$_2$CH(CONMe$_2$)–Br] (Figure S9). This byproduct can be regarded as a dimer ($A_MM_{DM}Br$) of methyl acrylate and N,N-dimethylacrylamide (M_{DM}) with a bromide terminal. Furthermore, in the case of the chloride (A_MA_MCl), highly selective amidation occurred rather than the S_N2 reaction, resulting in $A_MM_{DM}Cl$ due to the low leaving ability of chloride anion as well as the high activation of the ester moiety adjacent to the strongly electron-withdrawing chlorine atom.

This reaction was then applied to the synthesis of an ABCD tetramer possessing an acrylamide unit via the selective amidation of the methyl acrylate unit at the terminal chlorine in the ABCC tetramer ($VS_MA_MA_MCl$), which was prepared above, in the presence of various amines. Indeed, the terminal acrylate unit was selectively converted into the acrylamide unit in the presence of excess amounts of dimethylamine, n-propylamine, isopropylamine, and ethanolamine without any catalysts to give a series of the ABCD tetramers having M_{DM}, N-n-propylacrylamide (M_{NP}), N-isopropylacrylamide (M_{IP}), and N-hydroxyethylacrylamide (M_{HE}) as the D unit in good yield (Figure 2).

We thus synthesized a series of ab-type monomers with ABCC and ABCD vinyl monomer sequences possessing un-conjugated carbon–carbon double bonds and reactive carbon–chlorine bonds at their terminals. Here, all the carbon–chlorine bonds were activated by the adjacent electron-withdrawing substituent in the D unit and can generate elec-tron-deficient radicals, which are regarded as propagating rad-ical species derived from acrylate, acrylonitrile, acrylamide, and vinylidene chloride and are expected to add to the uncon-jugated C=C bond in the A unit in the presence of appropriate metal catalysts to induce step-growth radical polymerization.
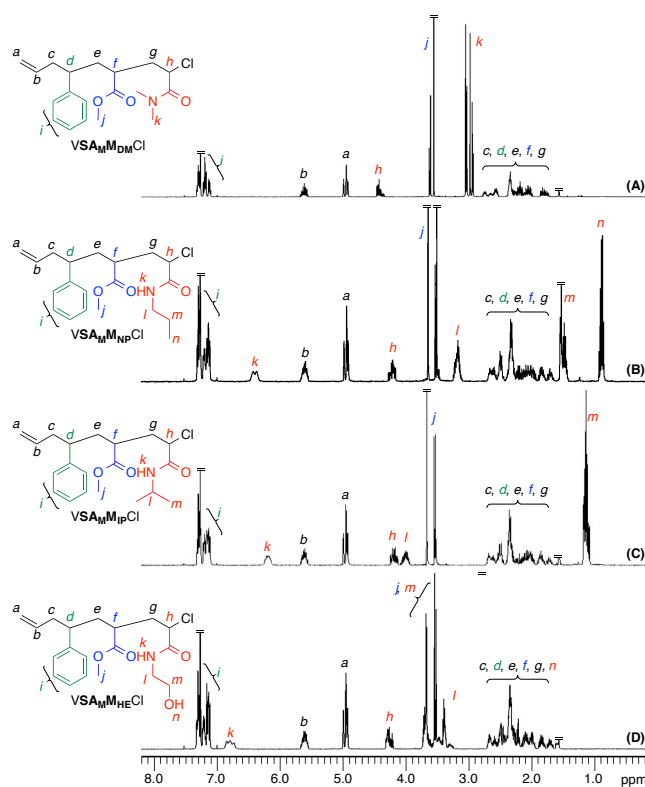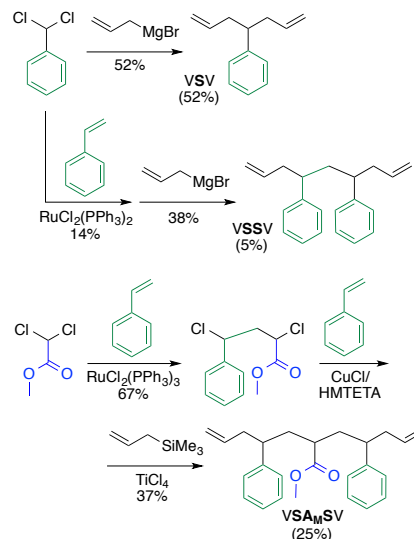

Figure 2. ^{1}H NMR spectra (CDCl$_3$, 25 °C) of a series of ab-type sequence-regulated monomers with ABCD sequences with acrylamide derivative units: (A) **VSA$_M$M$_{DM}$Cl**, (B) **VSA$_M$M$_{NP}$Cl**, (C) **VSA$_M$M$_{IP}$Cl**, (D) **VSA$_M$M$_{HE}$Cl**.

Synthesis of aa- and bb-Type Monomers for Higher-Order and Longer Vinyl Monomer Sequences. Metal-catalyzed step-growth radical polymerization also proceeds between pairs of aa- and bb-type monomers, which have two unconjugated C=C and two reactive C–Cl bonds, respective-ly.[73] This approach can provide higher-order and longer vinyl monomer sequences, even from relatively simple molecules, than those based on ab-type monomers, which require multiple synthetic steps for long sequences as stated above. One of the structural requirements for aa- and bb-type monomers is a symmetrical sequence, which rules out the opposite sequence in the resulting polymers.

For constructing symmetrical aa-type monomers with two unconjugated C=C bonds, double allylation of a symmetrical dihalide is one of the simplest methods (Scheme 5). We thus prepared a series of aa-type monomers that possess styrene and additional vinyl monomer units between two unconjugat-ed C=C bonds using similar ATRAs and double allylation.

The simplest aa-type monomer with one styrene unit between two unconjugated vinyl groups is α,α-diallyltoluene (**VSV**), which is regarded as a building block for the ABA sequence with a vinyl chloride-styrene-vinyl chloride sequence (**V$_C$SV$_C$**) upon reaction with a bb-type dichloride monomer as described below. This compound (**VSV**) was easily prepared via double allylation of α,α-dichlorotoluene by allylmagnesium bromide (Figure 3A).

Scheme 5. Synthesis of aa-Type Monomers with Two Un-conjugated C=C Bonds via Iterative ATRAs Followed by Double Allylations

[a]The values in percentages below arrows and in parentheses indi-cate yields for each reaction and total yields of final products, respectively.

Figure 3. ^{1}H NMR spectra (CDCl$_3$, 25 °C) of a series of aa-type sequence-regulated monomers with two unconjugated C=C bonds: (A) **VSV**, (B) **VSSV**, (C) **VSA$_M$SV**.

A longer aa-type monomer with two repetitive styrene units between the two unconjugated C=C bonds (**VSSV**) for the ABBA sequence was prepared by ruthenium-catalyzed single ATRA of styrene to either of the two equivalent C–Cl bonds

of α,α-dichlorotoluene followed by similar double allylation, which was performed by allylmagnesium bromide or by allyltrimethylsilane in the presence of TiCl$_4$ (Figure 3B). A longer building block for the ABCBA sequence possessing an additional monomer unit, i.e., methyl acrylate, in the middle of the molecule (VSA$_M$SV), was prepared from ClA$_M$Cl, to which iterative ATRAs of styrene were performed first by RuCl$_2$(PPh$_3$)$_3$ and second by CuCl/1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) followed by double allylation by allyltrimethylsilane in the presence of TiCl$_4$ (Figure 3C).

We thus successfully synthesized a series of aa-type monomers, which are regarded as building blocks for ABA trimer (VSV), ABBA tetramer (VSSV), and ABCBA pentamer sequences (VSA$_M$SV). In addition to these synthesized unconjugated dienes, a commercially available diolefin, 1,8-nonadiene, can be utilized as a building block for an ABBA sequence (VEEV, E: ethylene), as discussed later.

In contrast, the C–Cl bonds in bb-type monomers should be designed to be active enough to generate an electron-deficient radical, which can add to the unconjugated C=C bond in aa-type monomers. The simplest bb-type monomers are commercially available dichlorides such as methyl dichloroacetate (ClA$_M$Cl) and 2,2-dichloroacetonitrile (ClNCl), which were used as precursors for the ab-type monomers above. In addition to these building blocks for the methyl acrylate and acrylonitrile unimer unit, those for the dimer sequence, i.e., ClA$_M$A$_M$Cl (Figure 4A) and ClNNCl (Figure 4B), which have been prepared as precursors for VS$_M$A$_M$A$_M$Cl and VS$_M$NNCl, respectively (Scheme 2), can be used as bb-type monomers for higher-order building blocks.

Figure 4. ^{1}H NMR spectra (CDCl$_3$, 25 °C) of a series of bb-type sequence-regulated monomers with two reactive C–Cl bonds: (A) ClA$_M$A$_M$Cl, (B) ClNNCl, (C) ClNV$_C$EEV$_C$NCl.

Furthermore, a bb-type monomer with much higher-order and longer vinyl monomer sequences was prepared by ATRA between both commercially available 2,2-dichloroacetonitrile (ClNCl) and 1,8-nonadiene (VEEV) (Scheme 6), where the former was fed at a high ratio to the latter ([ClNCl]$_0$/[VEEV]$_0$ = 8.53/1.0 M). Because of the high feed ratio, as well as the higher reactivity of the original C–Cl bond in ClNCl than that

of the resulting C–Cl bond, both unconjugated C=C bonds in VEEV near-quantitatively and selectively react with each ClNCl molecule via double ATRAs to result in the building block (ClNV$_C$EEV$_C$NCl, V$_C$: vinyl chloride) for the ABCCBA-hexamer sequence (Figure 4C).

Scheme 6. Synthesis of a bb-Type Monomer (ClNV$_C$EEV$_C$NCl)

^{a}The values in percentages below arrows and in parentheses indicate yields for each reaction and total yields of final products, respectively.
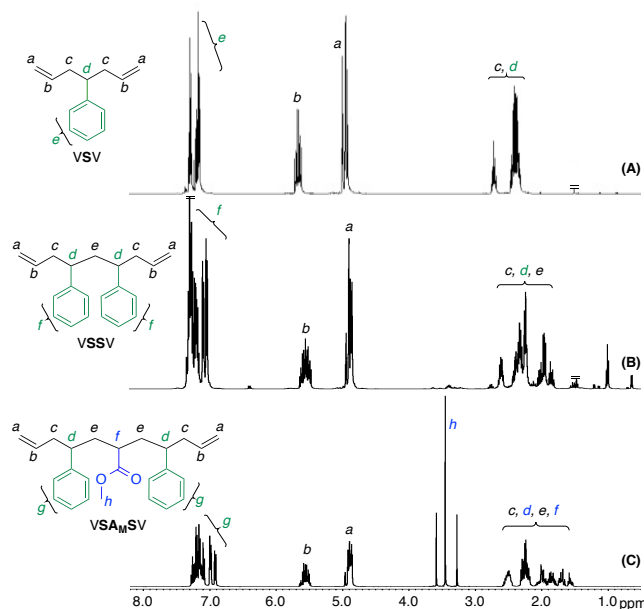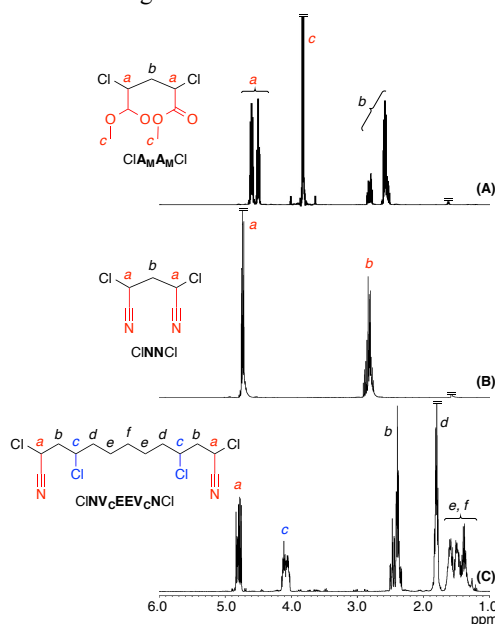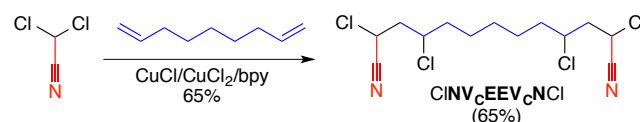
Thus, a series of bb-type monomers as building blocks for A-unimer (ClA$_M$Cl and ClNCl), AA-dimer (ClA$_M$A$_M$Cl and ClNNCl), and ABCCBA-hexamer units (ClNV$_C$EEV$_C$NCl) were prepared for subsequent step-growth radical polymerizations.

Metal-Catalyzed Step-Growth Radical Polymerization of ab-Type Monomers with ABCC and ABCD Tetramer Sequences. Step-growth radical polymerizations of a series of ab-type monomers with ABCC and ABCD sequences were investigated using transition metal catalysts that are effective for ATRAs and ATRPs.[66,74–78] Since sequence-regulated monomers are designed to possess a carbon–chlorine bond, which is similar to the dormant species in the ATRP of acrylate, acrylonitrile, acrylamide, or vinylidene chloride, appropriate catalysts could be those effective for the ATRP of the corresponding monomer given that these catalysts are at least effective for activation of the corresponding C–Cl bond. However, the deactivation process is different from the process in the ATRP because the abstracted chlorine should efficiently return to the different radical generated via radical addition to the unconjugated C=C bond in the sequence-regulated monomer. In addition, in many copper-mediated ATRPs, the C–Br bond, which has a higher reactivity than the C–Cl bond, is used.[66] Therefore, various transition metal catalysts and conditions should be examined to optimize metal-catalyzed step-growth radical polymerization depending on the structures of sequence-regulated monomers.

Figure 5. Time-conversion curves for metal-catalyzed step-growth radical polymerization of VSS$_M$A$_M$Cl with CuCl/PMDETA, HMTETA, or Me$_6$TREN in DMF at 60 °C and SEC curves of the polymers obtained with CuCl/PMDETA: [VSS$_M$A$_M$Cl]$_0$/[CuCl]$_0$/[ligand]$_0$ = 2000/200/800 mM.

For the acrylate-terminal ABCD tetramer (VSS_MA_MCl), ruthenium (RuCp*Cl(PPh$_3$)$_2$), iron (FeCl$_3$/PnBu$_3$), and copper (CuCl/HMTETA, tris[2-(dimethylamino)ethyl]amine (Me$_6$TREN), or *N,N,N',N'',N''*-pentamethyldiethyleneamine (PMDETA)) catalysts were used. Although all the catalysts induced polymerization (Table S1, entries 1–6), the reactions were generally slow due to the low reactivity of the C–Cl bond as well as the unconjugated vinyl group, in contrast to the ATRP of acrylates, in which highly reactive C–Br bonds are used and conjugated C=C bonds are polymerized. The molecular weights of the products, which were measured by size-exclusion chromatography (SEC) based on polystyrene standard calibration, were approximately 1000 to 2000. Among the various catalysts and conditions, CuCl with PMDETA in DMF at 60 °C led to relatively high conversion of C=C and C–Cl bonds (60–70%) (Figure 5).
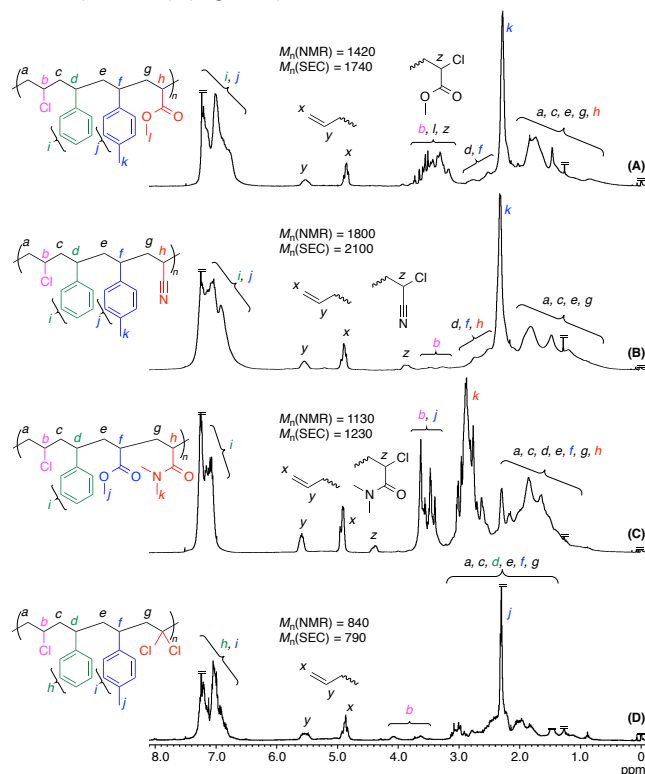

Figure 6. ^{1}H NMR spectra (CDCl$_3$, 55 °C) of polymers obtained by step-growth radical polymerization of ab-type monomers with ABCD sequences: (A) $(V_cSS_MA_M)_n$ obtained with CuCl/PMDETA in DMF at 60 °C (entry 6 in Table S1), (B) $(V_cSS_MN)_n$ obtained with CuCl/bpy in bulk at 100 °C (entry 13 in Table S1), (C) $(V_cSA_MM_{DM})_n$ obtained with CuCl/HMTETA in DMF at 80 °C (entry 20 in Table S1), (D) $(V_cSS_MV_{DC})_n$ obtained with FeCl$_2$/PnBu$_3$ in toluene at 60 °C (entry 26 in Table S1).

The ^{1}H NMR spectrum of the polymers obtained after purification by preparative SEC showed the characteristic peaks assignable to the embedded vinyl monomer units (styrene, *p*-methylstyrene, and methyl acrylate) and the vinyl chloride units formed upon step-growth polymerization (Figure 6A). In addition to the repeating sequence-regulated vinyl monomer units, peaks (*x* and *y*) of the terminal unconjugated vinyl group were clearly observed. The number-average molecular weight (M_n(NMR)) calculated from the peak intensity ratios of the terminal to the repeating units, assuming an ideal structure obtained by step-growth polymerization, was 1420, which was

comparable to that obtained by SEC (M_n(SEC) = 1740). These results indicate that the polymerization mainly proceeded via the expected step-growth polymerization mechanism to result in completely sequence-regulated vinyl copolymers consisting of four different ABCD monomer units, i.e., vinyl chloride-styrene-*p*-methylstyrene-methyl acrylate [$(V_cSS_MA_M)_n$], for the first time. However, the consumption of terminal C=C and C–Cl bonds was not exactly the same, suggesting that some side reactions occurred during the metal-catalyzed step-growth radical polymerization.

Then, the acrylonitrile-terminal monomers were polymerized. The bulk polymerization of the ABCC-sequenced monomer (VS_MNNCl) was first examined with CuCl in the presence of PMDETA, bpy, and 4,4'-dinonyl-2,2'-bipyridyl (dNbpy), which are effective ligands for the ATRP of acrylonitrile based on R–Br/CuBr-based systems.[71,72] These catalysts induced polymerization up to a relatively high conversion (60–100%) to result in polymers whose M_w(SEC)s were approximately 2000 to 3000 (entries 7–10 in Table S1). In particular, with CuCl/bpy, the terminal C–Cl bonds were consumed almost quantitatively (>99%), although the final conversion of unconjugated C=C was 76%. The resulting products had relatively high molecular weights (M_n(SEC) = 1800, M_w(SEC) = 3300), as shown in Figure 7A. However, with CuCl/PMDETA, the conversion was lower, and the high-molecular-weight fractions were apparently smaller than those obtained with CuCl/PMDETA (Figure 7B). These results indicate that CuCl/bpy is more appropriate for acrylonitrile-terminal monomers.
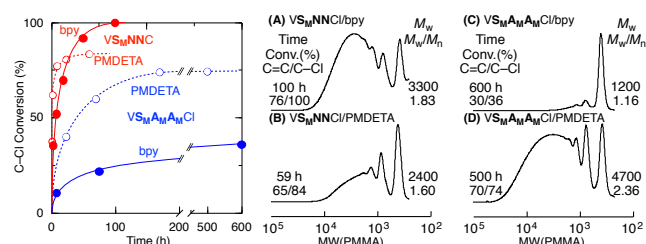

Figure 7. Metal-catalyzed step-growth radical polymerization of VS_MNNCl or $VS_MA_MA_MCl$ with CuCl/bpy or PMDETA in bulk at 100 or 60 °C, respectively: [CuCl]$_0$/[bpy]$_0$ = 200/1600 mM and 100 °C for (A) and (C); [CuCl]$_0$/[PMDETA]$_0$ = 200/800 mM and 60 °C for (B) and (D).

To evaluate the effects of the terminal vinyl monomer unit adjacent to the C–Cl bond on polymerization, a similar ABCC sequence-regulated monomer with an acrylate terminal ($VS_MA_MA_MCl$) was polymerized using the same catalysts in bulk (entries 11 and 12 in Table S1). As shown in Figure 7, the polymerization of the acrylate-terminal monomer was generally slower than that of the acrylonitrile counterpart under the same conditions due to the lower reactivity of the acrylate C–Cl terminal and the resulting acrylate radical to the unconjugated C=C bond. The CuCl/bpy catalyst was less effective for the acrylate monomer, whereas the CuCl/PMDETA catalyst was more suitable to produce higher-molecular-weight polymers (M_n(SEC) = 2000, M_w(SEC) = 4700) of the acrylate-terminal monomer (Figures 7C and 7D). These results show that the acrylonitrile-based monomer, for which bpy is a more suitable ligand, possesses higher reactivity in metal-catalyzed step-growth radical polymerization, whereas PMDETA is more suitable for acrylate.

The ABCD monomer with an acrylonitrile terminal (VSS_MNCl) was then polymerized with CuCl/bpy in bulk at 100 °C

(entry 13 in Table S1). Although the reaction was slower than that of the ABCC monomer (VS_MNNCl) under the same conditions (entry 10), the obtained polymers had similar molecular weights ($M_n(SEC) = 1800$, $M_w(SEC) = 3300$). The ^1H NMR spectra showed characteristic peaks of styrene, p-methylstyrene, acrylonitrile, and vinyl chloride units and small peaks (x and y) that were assignable to the terminal C=C and C–Cl bonds, respectively (Figure 6B). The $M_n(NMR)$ calculated from the terminal C=C was 1800, which was comparable to that by SEC ($M_n(SEC) = 2100$). In addition, the functionality of the terminal C–Cl bond relative to that of terminal C=C was calculated from the peak intensity ratios to be 0.84, although this value slightly deviated from the theoretical value for ideal step-growth polymerization. In total, the CuCl/bpy system was suitable for the acrylonitrile-terminal monomer to induce the expected step-growth polymerization and to result in a sequence-regulated vinyl copolymer consisting of four different monomer units, i.e., vinyl chloride-styrene-p-methylstyrene-acrylonitrile [$(V_cSS_MN)_n$].

The acrylamide-terminal ABCD monomers were then subjected to polymerization mainly using CuCl and multidentate amine-based ligands. Although copper-mediated living radical polymerization of acrylamide derivatives has been achieved, especially in aqueous media, in the presence of multidentate amine-based ligands, such as PMDETA, HMTETA, and Me6TREN,[79–82] aqueous systems are not appropriate for these sequence-regulated monomers, which are insoluble in water. Therefore, most of the polymerizations were carried out in bulk or in DMF (entries 14, 16–23 in Table S1).

The bulk polymerization of $VS_MA_MM_{DM}Cl$ with CuCl/PMDETA was first compared with that of the acrylate-terminal ABCC monomer, $VS_MA_MA_MCl$, which differs only in terminal unit, under the same conditions (entries 14 and 15). The polymerization of the acrylamide-terminal monomer was slightly slower and resulted in lower-molecular-weight products than that of the acrylate monomer. Furthermore, the consumption of C–Cl was faster than that of C=C. Similar results were obtained for the n-propylacrylamide-terminal monomer ($VS_MA_MM_{NP}Cl$) (entry 16).

The polymerization of $VS_MA_MM_{DM}Cl$ in DMF ($[M]_0 = 2.3$ M) was further examined using PMDETA, HMTETA, and Me6TREN under the same conditions (entries 17–19). All the polymerizations were generally slow and resulted in polymers with similar molecular weights ($M_w = 600$–800). Using HMTETA, all four acrylamide-terminal ABCD monomers were polymerized under the same conditions (entries 20–23). At a lower monomer concentration ($[M]_0 = 1.7$ M), the consumption of the C–Cl bond became faster. However, the consumption of the C–Cl bond was consistently higher than that of the C=C bond, suggesting that the resulting radical species not only reacted with the C=C bond but also underwent unfavorable reactions. The ^1H NMR spectrum of $(V_cSA_MM_{DM})_n$ obtained with CuCl/HMTETA in DMF at 80 °C showed the presence of terminal C=C and C–Cl bonds in addition to the sequenced units (Figure 6C). The $M_n(NMR)$ based on terminal C=C was 1130, which was close to that obtained by SEC ($M_n(SEC) = 1230$). The functionality of terminal C–Cl compared with that of C=C was 0.41, suggesting some loss of the C–Cl terminal due to side reactions. These results indicate that acrylamide-terminal monomers can be polymerized by CuCl/multidentate amine ligands, whereas ideal step-growth polymerization was difficult under the examined conditions.

The last ABCD sequence-regulated monomer, $VSS_MV_{DC}Cl$, which can generate vinylidene chloride radical, was then polymerized with copper, iron, and ruthenium catalysts (entries 24–28 in Table S1), although there are no reports on metal-catalyzed living radical polymerization and ATRP of V_{DC}, in contrast to numerous reports on vinyl chloride using copper-based systems.[83–85] The reactions with CuCl/PMDETA or HMTETA were sluggish in comparison to those of other monomers with different vinyl monomer terminals. However, with FeCl2/PnBu3, the reactions gave products with $M_w(SEC)$s of approximately 800–1000. The products showed the peaks of each monomer unit and terminal C=C (Figure 6D). The $M_n(NMR)$ based on the terminal C=C was 840 and was close to $M_n(SEC)$. RuCp*Cl(PPh3)2 induced consumption of the C=C up to 70% to give pruducts with similar molecular weights. Thus, vinylidene chloride terminals can be activated by metal catalysts, but it is difficult to obtain high-molecular-weight polymers.

Metal-Catalyzed Step-Growth Radical Polymerization of aa- and bb-Type Monomers. The above results for ab-type monomers suggest that CuCl/PMDETA and CuCl/bpy are suitable for the step-growth radical polymerization of monomers with acrylate and acrylonitrile C–Cl terminals, respectively. For the synthesis of higher-order and longer vinyl monomer sequences, step-growth radical polymerizations between aa-type monomers with two unconjugated vinyl groups and bb-type monomers with two acrylate or acrylonitrile C–Cl bonds were conducted using CuCl/PMDETA or bpy.

Acrylate-terminal dichlorides, i.e., methyl acrylate unimer and dichloride dimers (ClA_MCl and ClA_MA_MCl), were first used in conjunction with 1,8-nonadiene ($VEEV$) in the presence of CuCl/PMDETA in toluene at 60 °C (entries 1 and 2 in Table S2). The reactions occurred slowly in both cases to result in only low-molecular-weight products with $M_n = 400$–800.

Figure 8. Metal-catalyzed step-growth radical polymerization between $VEEV$ and ClNCl with CuCl/bpy in toluene at 100 °C: $[VEEV]_0/[ClNCl]_0/[CuCl]_0/[bpy]_0 = 2000/2000/100/800$ mM.

Then, acrylonitrile-terminal dichlorides, i.e., acrylonitrile unimer and dimer dichlorides (ClNCl and ClNNCl), were used in conjunction with the same diene ($VEEV$) in the presence of CuCl/bpy in toluene at 100 °C (entries 3 and 4 in Table S2). The reaction between ClNCl and $VEEV$ proceeded almost quantitatively to result in polymers with relatively high molecular weights ($M_w = 6000$) (Figure 8). At a middle stage of the reaction (Conv(C=C)/Conv(C–Cl) = 44%/48%), relatively large peaks assignable to the 1:1 (**A**) and 2:1 (**B**) adducts between ClNCl and $VEEV$ were observed in the SEC curves

with almost no higher-molecular-weight products. This result indicates the predominant formation of **A** and **B** due to the higher reactivity of one of the two reactive C–Cl bonds in Cl**N**Cl, which is activated by the other adjacent chlorine atom. Namely, the reactivity of the remaining reactive C–Cl bond in **A** and **B** was lower than that of the original Cl**N**Cl. The matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF-MS) of the resulting polymers showed a main series of peaks that are alternately separated by the molar masses of Cl**N**Cl (109.94) and V**EE**V (124.22) and are almost in agreement with the theoretical values for polymers with the expected structures and with sodium ions (Figure S10). The peaks attributed to the loss of a chlorine atom were observed and can be ascribed to laser-induced cleavage of the C–Cl terminal.

In contrast, the polymerization between the dichloride dimer (Cl**NN**Cl) and V**EE**V was very slow, which can be attributed to the coordination of two adjacent nitrile groups of Cl**NN**Cl to CuCl to decrease the activity. Similarly slow rates were observed for Cl**A$_M$A$_M$**Cl in comparison to Cl**A$_M$**Cl (entries 1 and 2 in Table S2). These results indicate that Cl**N**Cl is a suitable building block for the synthesis of sequence-regulated vinyl polymers via step-growth radical polymerization between aa- and bb-type monomers.

To make further higher-order and longer vinyl monomer sequences, Cl**N**Cl was employed with V**SS**V and V**SA$_M$S**V in the presence of CuCl and bpy in toluene at 100 °C (entries 5 and 6 in Table S2). In both cases, C=C and C–Cl were almost quantitatively consumed at nearly the same rate, suggesting that efficient radical additions between the aa- and bb-type monomers were mediated by CuCl/bpy (Figure 9). In addition, the M_n and M_w values gradually increased and reached 2,000 and 8,000, respectively. These results indicate that nearly ideal step-growth radical polymerization proceeded between the acrylonitrile-based C–Cl terminals and unconjugated C=C bonds in the presence of CuCl/bpy
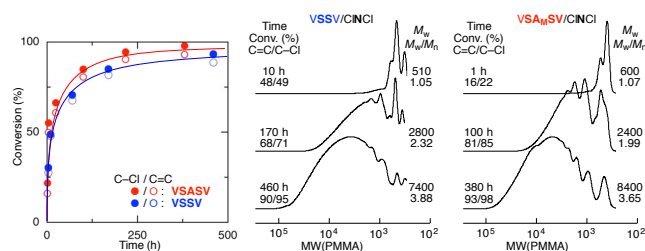

Figure 9. Metal-catalyzed step-growth radical polymerization between V**SS**V or V**SA$_M$S**V and Cl**N**Cl with CuCl/bpy in toluene at 100 °C: [V**SS**V]$_0$ or [V**SA$_M$S**V]$_0$/[Cl**N**Cl]$_0$/[CuCl]$_0$/[bpy]$_0$ = 1500/1500/100/800 mM.

Furthermore, the ^{1}H NMR spectra showed broad signals for the main-chain aliphatic protons, which originated from the vinyl monomer units and ranged from 1 to 4 ppm due to the various side-chain groups, and the characteristic aromatic protons of styrene units, indicating the formation of the ABBAC and ABDBAC sequence-regulated polymers consisting of embedded vinyl monomer units such as acrylonitrile (C), vinyl chloride (A), styrene (B), and methyl acrylate (D) (Figure 10). The terminal vinyl protons and the other terminal methine protons adjacent to the reactive C–Cl bond were clearly observed. The M_n(NMR) calculated from the terminal to main-chain protons were 2,500 and 3,600 for Cl**N**Cl/V**SS**V and

Cl**N**Cl/V**SA$_M$S**V, respectively, which were comparable to the M_n(SEC) values. These results indicate that the aa-type monomer with acrylonitrile-terminal C–Cl bonds and bb-type monomer with unconjugated C=C bonds are efficiently polymerized with CuCl/bpy to result in sequence-regulated vinyl polymers with unprecedented higher-order and longer vinyl monomer sequences and relatively high molecular weights.

Figure 10. ^{1}H NMR spectra (CDCl$_3$, 55 °C) of polymers obtained by step-growth radical polymerization between aa- and bb-type monomers: (A) (V$_C$**SS**V$_C$**N**)$_n$ obtained with CuCl/bpy in toluene at 60 °C (entry 5 in Table S2), (B) (V$_C$**SA$_M$S**V$_C$**N**)$_n$ obtained with CuCl/bpy in toluene at 60 °C (entry 6 in Table S2), (C) (V$_C$**SA$_M$S**V$_C$**N**V$_C$**EE**V$_C$**N**)$_n$ obtained with CuCl/bpy in toluene at 60 °C (entry 7 in Table S2)

The glass transition temperature (T_g) of poly(V$_C$**SA$_M$S**V$_C$**N**), which has a relatively high molecular weight (M_w(SEC) = 15000, M_n/M_n = 1.76), fractionated by preparative SEC was 80.5 °C (Figure S11). This value was nearly the same as the weighted average T_g value, 80 °C, for two poly(vinyl chloride)s (80 °C), two polystyrenes (100 °C), one poly(methyl acrylate) (10 °C), and one polyacrylonitrile (110 °C).[69] The effects of monomer sequences on thermal properties should be examined in more detail.

A long monomer sequence was investigated using ClNV_CEEV_CNCl with a hexamer sequence and VSA_MSV with a pentamer sequence. Although the reactivity of the C–Cl bond is lower than that in ClNCl, the aa-type monomer sufficiently reacted with the bb-type monomer to induce the almost simultaneous and quantitative consumption of both the C–Cl and C=C bonds at a proportion higher than 90% (entry 7 in Table S2). The final M_n and M_w values were 2900 and 7500, respectively. The ^{1}H NMR spectrum showed similarly complicated main-chain aliphatic protons between 1 and 4 ppm and characteristic aromatic protons. Small signals were observed for the terminal vinyl and chloride-methine protons, where the ratio of C=C to C–Cl was 1.06 (Figure 10). In addition, the M_n(NMR) calculated from the terminal to main-chain protons was 2300, which was close to the M_n(SEC) value. These results indicate the formation of ABDBACAEEAC sequence-regulated vinyl polymers consisting of 11 embedded vinyl monomer units, including acrylonitrile (C), vinyl chloride (A), styrene (B), methyl acrylate (D), and ethylene (E).

CONCLUSIONS

A series of sequence-regulated ab-type monomers with embedded ABCC and ABCD vinyl monomer sequences between the terminal unconjugated C=C and reactive C–Cl bonds were successfully prepared via iterative single vinyl monomer additions mediated by radical or cationic species followed by selective allylation and, if necessary, amidation. Alternatively, a series of aa- and bb-type monomers with symmetrical monomer sequences between both C=C or both C–Cl bonds, respectively, were prepared by similar reactions. The embedded vinyl monomer units included styrenes, acrylates, acrylonitrile, acrylamides, vinyl chloride, vinylidene chloride, and ethylene. Transition metal-catalyzed step-growth radical polymerization proceeded for the ab-type monomers or a pair of aa- and bb-type monomers to result in sequence-regulated vinyl polymers, though the reaction rates and resulting polymer molecular weights depended on the monomers. The acrylate C–Cl terminal was more suitable for providing higher molecular weight polymers due to its higher reactivity. This strategy thus enabled the construction of structures equivalent to sequence-regulated vinyl polymers with higher-order and longer vinyl monomer sequences and moderate molecular weights using vinyl monomers as s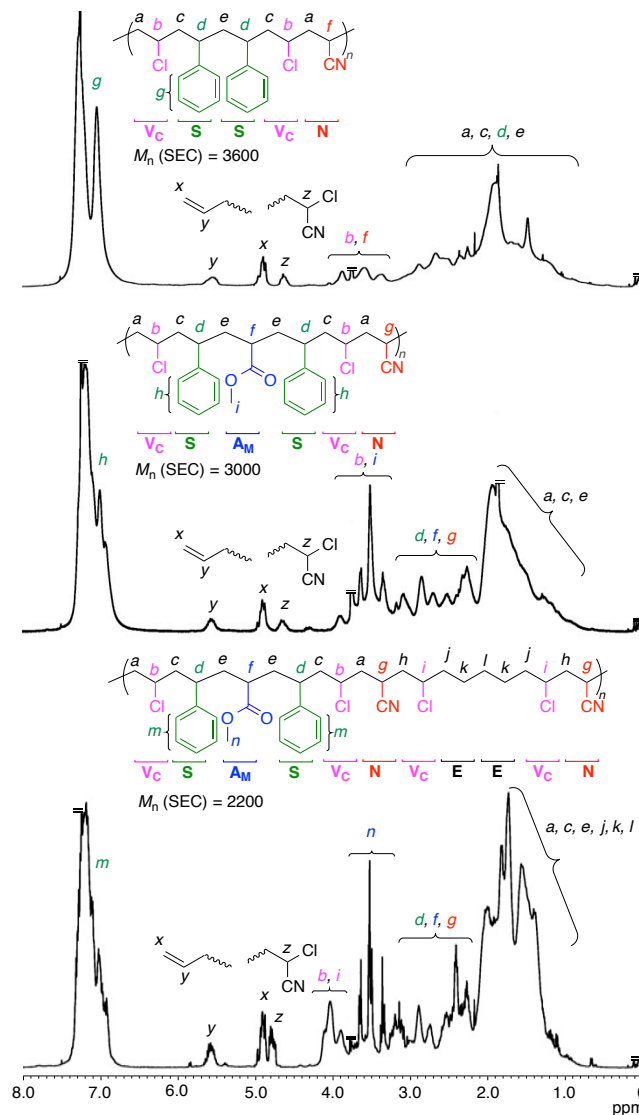tarting materials. Further progress in terms of more efficient step-growth radical polymerization will enable the synthesis of high-molecular-weight polymers, reveal the effects of vinyl monomer sequences on the properties of the polymers and finally contribute to the development of novel vinyl polymer technologies.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedure and supplementary data (PDF)

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Notes
The authors declare no competing financial interest.

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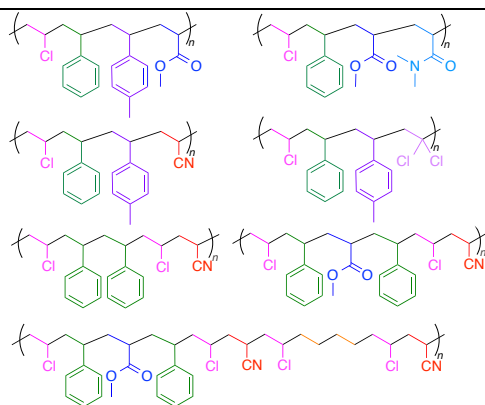
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