Copolymerization

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Interconvertible Living Radical and Cationic Polymerization through Reversible Activation of Dormant Species with Dual Activity**

Hiroshi Aoshima, Mineto Uchiyama, Kotaro Satoh, and Masami Kamigaito**

***Abstract:** The polymerization of vinyl monomers generally requires the selection of an appropriate single intermediate, whereas in copolymerization, the selection of the comonomer is limited by the intermediate. Herein, we propose interconvertible dual active species that can connect comonomers through different mechanisms to produce specific comonomer sequences in a single polymer chain. More specifically, two different stimuli, that is, a radical initiator and a Lewis acid, are used to activate the common dormant C–SC(S)Z group into radical and cationic species, thereby inducing interconvertible radical and cationic copolymerization of acrylate and vinyl ether to produce a copolymer chain that consists of radically and cationically polymerized segments. The dual reversible activation provides control over molecular weights and multiblock copolymers with tunable segment lengths.*

A chemical reaction often proceeds via a specific intermediate, such as a cation, anion, and radical, thereby converting a starting material into a product, preferably with high selectivity and yield. Different intermediates are believed to be fundamentally incompatible, because they are supposed to interfere with each other and are usually unnecessary in the formation of a desired product based on a single step. This observation is also true for chain-growth polymerization, in which an appropriate intermediate, initiator, or catalyst, is chosen depending on the monomer type in order to produce the desired polymer chain through repetitive reactions between the reactive intermediate and the monomers.[1] In order to obtain polymers that possess the desired properties, different monomers may be copolymerized, thereby changing the properties of the resulting polymer; accordingly, copolymerizations are widely employed for many common polymers. However, the selection of comonomers is limited, because not every monomer can be polymerized with every intermediate. One plausible strategy to ease this restriction is the conversion of a reactive intermediate into another one during the polymerization process. This alteration would enable the synthesis of novel copolymers with unprecedented comonomer sequences that have not been accessible using a single intermediate. However, the direct interconversion of intermediates during polymerization has not been fully achieved because of the rapid rate of propagation. In conventional chain-growth polymerization, the reactive intermediate propagates into a growing polymer chain immediately after its formation, and then undergoes termination and/or chain-transfer reactions, which result in a "dead" polymer. Thus, the propagating species has almost no chance of interconversion into another species because of its generally short lifetime and unstable nature. Although one-way conversions during copolymerization have been reported in the synthesis of block copolymers,[2–13] most remain incomplete as a result of low efficiency and/or are limited to one occurrence because of an irreversible transformation.

Recent decades have seen significant developments in "living" or controlled polymerizations,[14,15] which proceed via various single intermediates, such as anionic, cationic, radical, and coordinating species. In most of these modern "living" polymerizations, that is, reversible deactivation polymerization according to the terminology recommended by the IUPAC,[16] the reactive intermediates are transiently converted or reversibly deactivated into the dormant covalent species. That is, the short-lived and unstable intermediates are reversibly deactivated for some time, resulting in dormant covalent species, which can propagate again after reversible activation. Such a reversible interconversion between the dormant and active species affords an almost equal opportunity of chain growth for all of the initiator or polymer molecules, resulting in polymers with approximately equivalent chain lengths. Thus, the dormant species play an important role in controlling the chain length of the resulting polymers by extending the lifetime of the chain, including its dormant period. Contributions from the dormant species are necessary for the precise control of the molecular weight, especially in the cationic[17–20] and radical[21–26] polymerization of vinyl ether monomers, in which both of the propagating species, that is, carbocationic and radical intermediates, are short-lived and unstable.

Here, to copolymerize different types of monomers that cannot be copolymerized via a single intermediate, we propose the activation of the dormant species into two different intermediates using dual reversible activation (Scheme 1). Specifically, one intermediate is deactivated into the dormant state and then activated into another one using a different route. To realize this strategy, the method

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[*] Dr. H. Aoshima, M. Uchiyama, Prof. Dr. K. Satoh,
Prof. Dr. M. Kamigaito
Department of Applied Chemistry, Graduate School of Engineering,
Nagoya University
Furo-cho, Chikusa-ku, Nagoya 464-8603 (Japan)
E-mail: satoh@apchem.nagoya-u.ac.jp
kamigait@apchem.nagoya-u.ac.jp

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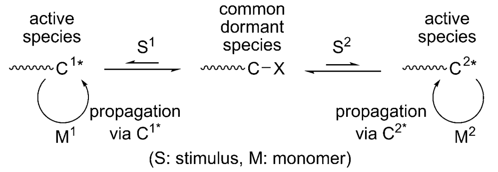
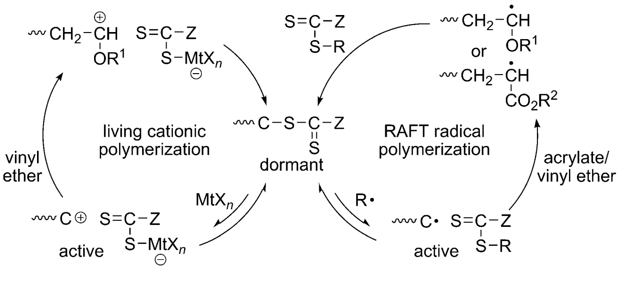


Scheme 1. Concept for concurrent copolymerizations proceeding through the reversible activation of common dormant species by two different stimuli.

required at least one common dormant species and two different stimuli, which activate the common dormant state into different intermediates. Additionally, both intermediates and stimuli have to be compatible.[27]

To demonstrate the feasibility of this strategy, we report the interconvertible, living cationic and radical polymerization of vinyl ether and acrylate monomers using a thioester as the common dormant species and a Lewis acid catalyst and an azo initiator as the stimuli to generate the carbocation and carboradical, respectively, from the dormant thioester (Scheme 2). The selection of components was based on the following facts: the vinyl ether monomer can be homopolymerized only via a cationic intermediate, which cannot polymerize acrylate monomers at all, while a radical intermediate can efficiently homopolymerize acrylate monomers and also copolymerize vinyl ether monomers to an extent. Thioester compounds were extensively employed as reversible addition–fragmentation chain-transfer (RAFT) agents for controlling the radical polymerization of various vinyl ether monomers, including acrylate monomers, through the reversible activation of the dormant thioester by a radical species that originates from the radical initiator.[24] Additionally, a similar thioester can be reversibly activated into the carbocationic species in the presence of a Lewis acid catalyst to induce the living cationic homopolymerization of vinyl ether monomers, as we reported recently.[11]



Scheme 2. Mechanism of concurrent radical and cationic polymerization of acrylate and vinyl ether monomers through reversible activation of the dormant thioester by radical species (R$^\bullet$) and Lewis acids (MtX$_n$).

We examined this strategy by using a trithiocarbonate (**1** in Figure 1) capable of generating cationic and radical intermediates in conjunction with EtAlCl$_2$ and 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70), respectively, to copolymerize an equimolar mixture of isobutyl vinyl ether (IBVE) and methyl acrylate (MA) monomers in toluene at 20 °C.

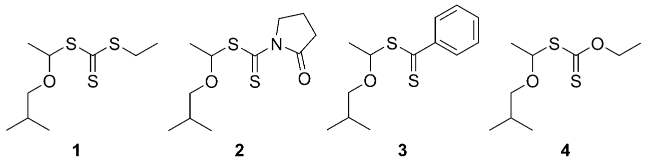


Figure 1. Vinyl ether derived RAFT agents used in this study.

As a control experiment for the copolymerization with both stimuli, a single stimulus, that is, the Lewis acid or the radical initiator, was first used with a mixture of IBVE and MA in the presence of **1**. When EtAlCl$_2$ was combined with **1**, IBVE was consumed quantitatively without the consumption of MA, indicating that only the cationic homopolymerization of IBVE occurred (Supporting Information, Figure S1a). In contrast, when V-70 was used, MA was consumed quantitatively along with the slower consumption of IBVE, the conversion of which finally reached approximately 30 % (Figure S1b), thus indicating that radical copolymerization of MA occurred with a small amount of IBVE. The polymers obtained in both control experiments showed unimodal size-exclusion chromatography (SEC) curves and controlled molecular weights, which increased in direct proportion to the conversion of the monomers and agreed well with the calculated values, assuming that one molecule of **1** generates one polymer chain (Figure S2a). Thus, the dormant C−S bond of trithiocarbonate is suitable for both cationic and radical reversible deactivation polymerization reactions when catalyzed by a Lewis acid and a radical species, respectively; both reactions proceed at similar rates under the optimized conditions.

Next, both catalysts, EtAlCl$_2$ and V-70, were used to induce the simultaneous and quantitative consumption of both monomers, with a slightly faster rate for IBVE than MA (Figure S1c). The consumption rates of IBVE and MA in the presence of both catalysts were almost the same as those of IBVE with EtAlCl$_2$ and MA with V-70. These kinetic results suggest that both the cationic and radical polymerization reactions proceeded in the presence of both catalysts without interference. Furthermore, the resulting polymers possessed unimodal SEC curves and controlled molecular weights that agreed well with the calculated values (Figure 2). Thus, the dormant trithiocarbonate group is simultaneously activated by both a Lewis acid and a radical species to induce simultaneous living cationic and radical polymerizations through the reversible deactivation process.

The ^{1}H and ^{13}C NMR analyses of these products further support the hypothesis that the concurrent living cationic and radical polymerizations proceeded via the dual active intermediate. The ^{1}H NMR spectrum of the polymers obtained by using both catalysts (Figure S3c) is essentially a superposition of the two spectra of the homopolymer of cationically prepared IBVE (Figure S3a) and the copolymer of radically prepared MA and IBVE (Figure S3b), thus indicating that the copolymers obtained using both catalysts possess sequences

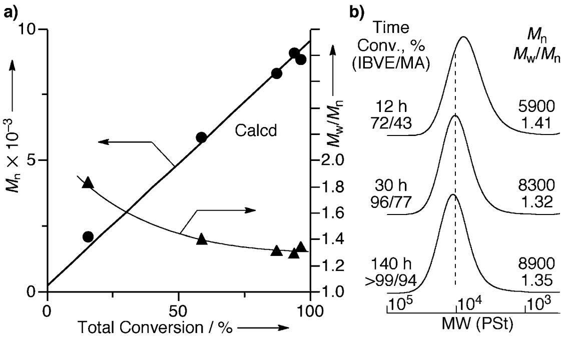


Figure 2. Interconvertible polymerization of an equimolar mixture of IBVE and MA in toluene at 20 °C. a) Number-average molecular weight (M_n) and M_w/M_n (where M_w is the weight-average molecular weight) with respect to the total conversion of the monomers. b) Size-exclusion chromatography curves of polymers obtained with $EtAlCl_2$ and V-70 at varying monomer conversions in the polymerization. $[IBVE]_0 = [MA]_0 = 2.0$ M; $[\mathbf{1}]_0/[EtAlCl_2]_0/[V\text{-}70]_0 = 40/2.5/10$ mM; $[EtOAc]_0 = 1.0$ M.

that were polymerized via both cationic and radical intermediates.

The ^{13}C NMR spectra (Figures 3 and S4) give detailed information regarding the monomer sequences. The carbonyl carbon atoms of the MA units split into three resonances because of the possible triad monomer sequences, that is, M**M**M, I**M**M (M**M**I), and I**M**I (M = MA, I = IBVE), in which M**M**M is higher with both catalysts (Figure 3 c) than with V-70 alone (Figure 3 b). This result indicates that the number of radically copolymerized IBVE units was lower with both catalysts because of the simultaneous consumption of IBVE by the cationic intermediate. As for the carbon atoms of the vinyl ether units, the chemical shifts of the main-chain methine carbon atoms of the IBVE units are distinctly different for I**I**I (74 ppm) and M**I**M (76 ppm), which were obtained for the cationic (Figure 3 a) and radical propagations (Figure 3 b), respectively. Between the two absorptions, which can also be observed for the polymers obtained using both catalysts (Figure 3 c), a new resonance appears at 75 ppm. This signal can be assigned to another triad, either the I**I**M or M**I**I sequence, thus indicating that the intermediate is converted from a cation to a radical or from a radical to a cation in this triad because the II and IM (or MI) sequences only form through cationic and radical propagations, respectively.

Figure 4 a shows the cumulative contents of the triad comonomer sequences (M**M**M, I**M**M (M**M**I), I**M**I, I**I**I, I**I**M (M**I**I), and M**I**M), which were obtained by the integration of these resonances against the monomer conversions. These values were then employed to calculate the cumulative contents of the cationic and radical propagations. As shown in Figure 4 b, the contents of the cationic propagations were higher than the radical propagations in the early to middle stages of polymerization, which is also supported by the slightly faster consumption of IBVE than MA, as shown in Figure S1c. However, the radical propagation finally became larger because IBVE was radically copolymerized with MA. More importantly, the number of interconversions per chain (N_{conv}) was calculated using the content of I**I**M (M**I**I) and the number-average degree of polymerization (DP_n) at each conversion. As shown in Figure 3 b, N_{conv} increased with the monomer conversion, finally reaching 4.66 when DP_n increased to 96.9. This result indicates that interconversion occurred approximately five times during 100 monomer propagations per chain under typical conditions. As discussed later, N_{conv} depends on many factors, including the dormant species, Lewis acid, and radical initiator, as well as the concentrations, temperature, and solvents. The number-aver-

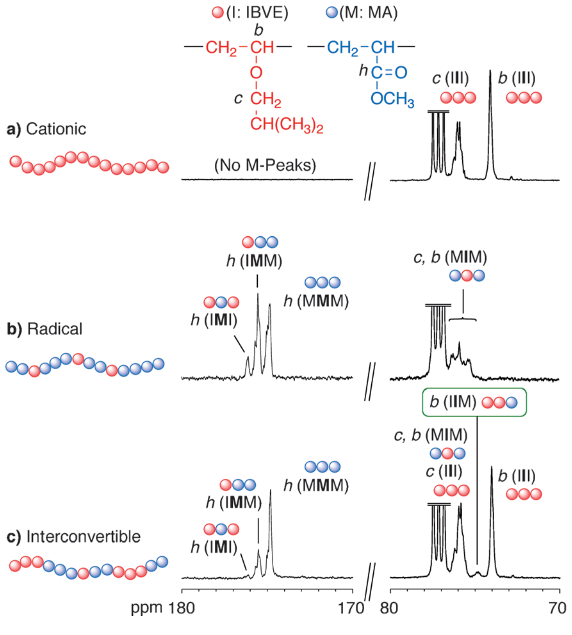


Figure 3. ^{13}C NMR spectra (in $CDCl_3$ at 55 °C) of polymers obtained in a) cationic, b) radical, and c) interconvertible polymerization of IBVE and MA. $[IBVE]_0 = [MA]_0 = 2.0$ M; $[\mathbf{1}]_0 = 40$ mM; $[EtAlCl_2]_0/[V\text{-}70]_0 = 2.5/0$ (a), 0/10 (b), 2.5/10 mM (c); $[EtOAc]_0 = 1.0$ M; in toluene at 20 °C. a) Conversion(IBVE/MA) = 99 %:2 %, M_n(SEC) = 5100, $M_w/M_n = 1.42$. b) Conversion(IBVE/MA) = 31 %:94 %, M_n(SEC) = 7300, $M_w/M_n = 1.29$. c) Conversion(IBVE/MA) = > 99 %:94 %, M_n(SEC) = 9600, $M_w/M_n = 1.31$.

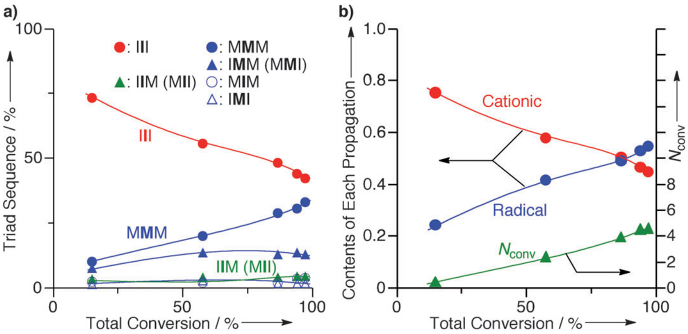


Figure 4. Interconvertible cationic and radical polymerization of IBVE and MA. a) Triad monomer sequences of copolymers obtained in the interconvertible radical and cationic polymerization in Figure 1 with respect to total monomer conversion (where I and M mean IBVE and MA monomer units). b) Cumulative contents of radical and cationic propagations and number of interconversions per chain (N_{conv}) in the copolymerizations with respect to total monomer conversion. $[IBVE]_0 = [MA]_0 = 2.0$ M; $[\mathbf{1}]_0/[EtAlCl_2]_0/[V\text{-}70]_0 = 40/2.5/10$ mM; $[EtOAc]_0 = 1.0$ M; in toluene at 20 °C.

age degree of propagation during one cycle of interconversion, that is, the average segment length ($n = 20.8$), was also calculated by DP_n/N_{conv}, and became slightly shorter as the polymerization proceeded or as the monomer concentration decreased (Figure S5).

The result of interconvertible copolymerization was further supported by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF-MS). The signals of the copolymers obtained using both catalysts (Figure S6c) are separated by 14 Da, that is, the molar mass difference between IBVE (100) and MA (86), thus indicating that most of the polymer chains are copolymers. Additionally, the spectral shape varies slightly for the copolymers obtained only via the radical intermediate (Figure S6b), which differs significantly from the result obtained for the homopolymer of IBVE (Figure S6a). In the radical RAFT copolymerization (Figure S6b), a series of polymer chains with the same total number of monomer units but a different number of each unit type regularly appears in a mountain-like shape because of the nature of the statistical distribution,[28] which is governed by the reactivity ratios of the monomers in radical copolymerization. However, this statistical distribution is hampered by the concurrent cationic propagation reaction, which results in a flattened spectral pattern (Figure S6c).

The obtained polymers were also analyzed by high-performance liquid chromatography (HPLC), in which the solvent polarity was gradually increased by increasing the ratio of THF to *n*-hexane, which were used as the eluent. The homopolymer of IBVE obtained through cationic polymerization (Figure S7a) eluted faster than the copolymer of MA and IBVE obtained through radical copolymerization (Figure S7b) because of the lower polarity of IBVE relative to that of MA. The copolymers obtained using both catalysts eluted at almost the same or a slightly faster rate than the copolymers obtained through radical copolymerization and showed broader peaks (Figure S7c). Thus, most of the products obtained when using both catalysts are copolymers that contain a larger number of IBVE units than the products obtained using only radical copolymerization because of the concurrent cationic homopolymerization of IBVE. However, a very small peak at a shorter elution time suggests a slight amount of remaining homopolymer of IBVE, which was not converted into radical polymerization.

The frequency of interconversion as well as the rate of polymerization is dependent on the Lewis acid catalyst. When the copolymerization was carried out with a weaker Lewis acid, $ZnCl_2$,[20] instead of $EtAlCl_2$, the consumption of IBVE became slower and closer to that of MA (Figure S8b). The resulting products showed narrower molecular weight distributions (MWDs) ($M_w/M_n = 1.25$) and controlled M_n, which agreed well with the calculated values. N_{conv} increased to 7.24 (Figure S9b), which is larger than that obtained with $EtAlCl_2$ (4.66, see above). The average segment length (n) was thus calculated to be $n = 12.8$. With $ZnCl_2$, the interconversion became more frequent, partially because of the reduced rate of cationic polymerization. In contrast, another Lewis acid, $FeCl_3$, inhibited the radical polymerization of MA, which resulted in only a homopolymer of IBVE as a result of redox activity (Figure S8c).

A series of RAFT (R-SC(S)Z) agents consisting of the same R (R = 2-isobutoxyethyl) and different Z (Z = 2-pyrrolidonyl (**2**), phenyl (**3**), ethoxy (**4**)) groups (Figure S11 and S12) were also examined in the presence of both V-70 and $ZnCl_2$ under the same conditions. With **2** and **4**, both monomers were consumed at almost the same rate as with **1** (Figure S12). The M_n of the products increased in direct proportion to the monomer conversion and agreed well with the calculated values (Figure S13a). However, the MWDs were slightly broader with **2** ($M_w/M_n = 1.43$) and were bimodal with **4** (Figure S13b), suggesting that the interconversion was slightly slower with **2** and significantly slower with **4**. ^{13}C NMR analyses also indicate that the **IIM** (**MII**) signal is smaller with **2** and almost nonexistent with **4** (Figure S14a) and that N_{conv} is smaller with **2** (3.06) and significantly smaller with **4** (≤ 0.83) (Figure S14b). This result is due to the electron-donating Z groups, which retard the addition of radical species to the RAFT moiety, thereby resulting in slow activation or interconversion. More specifically with **4**, the cationic and radical polymerization processes proceeded separately, almost without transformation, resulting in bimodal MWDs. Using another RAFT agent, **3**, no consumption of MA occurred (Figure S12c). With **3**, no radical homopolymerization of MA occurred, most likely because of the stable intermediate derived from the dithiobenzoate-type RAFT agent.[24] Thus, the choices of RAFT agent and Lewis acid are crucial for achieving successful interconvertible polymerization.

The interconversion number, that is, the average segment length in the copolymers affects the thermal properties of the resulting polymer (Figure 5). The copolymers with low N_{conv} (3.06 and ≤ 0.83) or high average segment lengths ($n \geq 30$) showed two glass transition temperatures (T_g), below −15 °C and at approximately 5 °C, originating from T_g of poly(IBVE) and poly(MA-*stat*-IBVE), respectively. However, with a high N_{conv} (7.24) or low n (12.8), only one T_g was observed (−14 °C) because of the presence of miscible short segments. Thus, novel copolymers with tunable properties can be obtained through interconvertible cationic and radical polymerizations.

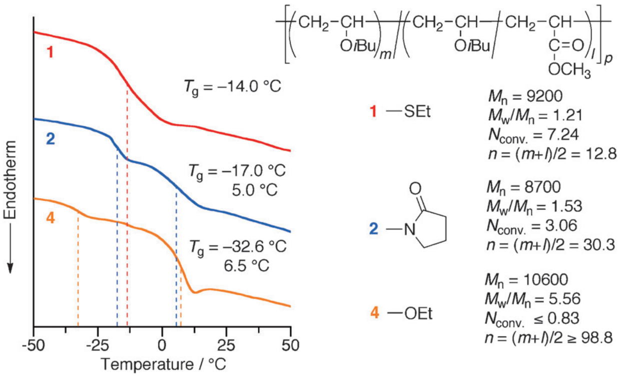


Figure 5. Differential scanning calorimetry (DSC) curves of polymers obtained in the interconvertible cationic and radical polymerization of IBVE and MA with various RAFT agents in the presence of both $ZnCl_2$ and V-70 in toluene at 20 °C. $[IBVE]_0 = [MA]_0 = 2.0$ M; [RAFT Agents]$_0 = 40$ mM; $[ZnCl_2]_0 = 2.5$ mM, $[V\text{-}70]_0 = 10$ mM, $[EtOAc]_0 = 1.0$ M.

Another combination of monomers, IBVE and methyl methacrylate (MMA) in place of MA, was also examined with **1**/$ZnCl_2$/V-70 under similar conditions (Figure S15). The copolymerization at a monomer feed ratio of 1:1 resulted in bimodal MWDs, thus suggesting slower interconversion as a result of the lower radical copolymerizability of IBVE with MMA. However, unimodal MWDs were attained at a higher IBVE feed ratio (IBVE/MA = 3:1), which enhances the relative formation of an IBVE chain end possessing both radical and cationic reactivity. Thus, the selection of monomers and conditions is important for the interconvertible polymerization, and more detailed studies including other combinations are now under way in our laboratory.

Herein, we demonstrated the first concurrent radical and cationic polymerizations that proceed via interconvertible dual active species for the production of multiblock copolymers with controlled chain and segment lengths (Figure S16). This method provides a new strategy for producing copolymers comprised of different types of monomers that cannot be copolymerized via a single intermediate.

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