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Microflow System Controlled Carbocationic Polymerization of Vinyl Ethers

Aiichiro Nagaki,[a] Takeshi Iwasaki,[a] Kohsuke Kawamura,[a] Daisuke Yamada,[a]
Seiji Suga,[a] Tuyoshi Ando,[b] Mitsuo Sawamoto,[b] and Jun-ichi Yoshida*[a]

Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday

Abstract: A "cation pool" of an *N*-acyliminium ion was found to serve as an effective initiator of cationic polymerization of vinyl ethers in a microflow system consisting of two micromixers (IMM micromixer) and two microtube reactors. The cationic polymerization of *n*-butyl vinyl ether in CH_2Cl_2 at −78 °C led to very narrow molecular weight distribution ($M_w/M_n = 1.14$). The molecular weight (M_n) increased linearly with an increase in monomer/initiator ratio. The carbocationic polymer end was effectively trapped by allyltrimethylsilane. Additionally, the synthesis of block polymers was accomplished by the present microflow system controlled method. The polymerization was also conducted using commercially available trifluoromethanesulfonic acid (TfOH) as an initiator. A high level of molecular weight control was attained even at −25 °C. The TfOH-initiated polymerization could be conducted using a microflow system based on T-shaped micromixers, which serves as a practical tool for microflow system controlled carbocationic polymerization.

Keywords: block copolymers · cations · microreactors · polymerization · polymers

Introduction

Cationic polymerization is one of the most fundamental methods for synthesizing polymers. Although there are several types of cationic polymerization, cationic polymerization of vinyl monomers such as vinyl ethers is very popular. One of the most important breakthroughs in cationic polymerization is the discovery of living cationic polymerization,[1–2] which enables excellent molecular weight and molecular weight distribution control. The inherent and serious drawback of cationic vinyl polymerization is instability of the carbocationic intermediates, which causes chain transfer and leads to the formation of polymers with a broad molecular weight distribution. In living cationic polymerization, however, the carbocationic intermediate is stabilized by the interaction with a suitably nucleophilic counter anion or an externally added Lewis base, although such stabilization causes a deceleration in the propagation.[3–6]

Recently, we have found another way to control molecular weight and molecular weight distribution in cationic polymerization of vinyl ethers with the use of microflow systems.[7,8] Chemical synthesis in microflow systems has received significant interest from both academia and industry.[9,10] Prominent features of microflow systems include a fast mixing, stemming from a short diffusion time, and fast heat transfer, by virtue of a high surface/volume ratio, which are advantageous for increasing the selectivity of the chemical reactions.[11] A short residence time in the micro channel is beneficial for controlling the highly reactive intermediates.[12] Taking advantage of such features of microflow systems has allowed various chemical reactions for organic synthesis to be developed.[13] Polymer synthesis is another fascinating field where an application of microflow systems may be facilitated.[14] Major advantages of polymerization using microflow systems include the control of the molecular weight of polymers by modulating the residence time in the reactor. It is also noteworthy that the continuous microflow systems are suitable for producing libraries of polymers for high-throughput evaluation. There have been numerous reports on the use of microflow systems for the polymerization

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[a] Dr. A. Nagaki, Dr. T. Iwasaki, K. Kawamura, D. Yamada,
Dr. S. Suga, Prof. Dr. J. Yoshida
Department of Synthetic and Biologycal Chemistry, Graduate School of Engineering, Kyoto University Nishikyo-ku, Kyoto, 615-8510 (Japan)
Fax: (+81) 75-383-2727
E-mail: yoshida@sbchem.kyoto-u.ac.jp

[b] Dr. T. Ando, Prof. Dr. M. Sawamoto
Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University Nishikyo-ku, Kyoto, 615-8510 (Japan)

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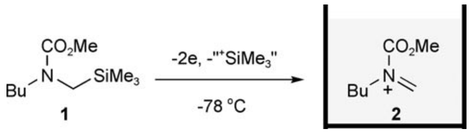
including radical polymerization,[15] coordination polymerization,[16] polycondensation reaction,[17] and polymerization of amino acids.[18]

We have reported that fast living/controlled cationic polymerization could be achieved in a microflow system using a cation pool[19] as initiator, without adding any nucleophilic counter anion or Lewis base.[7] A high degree of molecular weight and molecular weight distribution control can be attained without the deceleration inherent in the dynamic equilibrium between active and dormant species. Furthermore, we have also reported that cationic polymerization using a strong Brønsted acid, such as TfOH (CF_3SO_3H), can be accomplished in a highly controlled manner in a microflow system.[8] These observations may open a new aspect of living cationic polymerization, and herein we report full details of these studies.

Results and Discussion

Cationic Polymerization by an *N*-Acyliminium Ion Pool using a Macrobatch Reactor

As a "cation pool", we chose to study the *N*-acyliminium ion **2**. This is generated from *N*-methoxycarbonyl-*N*-(trimethyl silylmethyl)butylamine **1**, having a silyl group as an electroauxiliary,[20] by low temperature electrochemical oxidation in CH_2Cl_2, and accumulates in a solution (cation pool; Scheme 1). The *N*-acyliminium ion **2** does not have a substituent on the iminium carbon and is not sterically demanding. Therefore, it seems to be suitable as an initiator for cationic polymerization. The counteranion of **2** was the tetrafluoroborate anion (BF_4^-) derived from the supporting electrolyte (Bu_4NBF_4) for the electrochemical oxidation. The formation of **2** as a single species was indicated by NMR (^{1}H NMR: $\delta = 8.56$ and 8.83 ppm arising from the methylene protons, ^{13}C NMR: $\delta = 177.0$ ppm arising from the methylene carbon).



Scheme 1. Generation of an *N*-acyliminium ion pool (**2**) from its precursor **1**.

Abstract in Japanese:

カチオンプール法により発生させた*N*-アシルイミニウムイオンを開始剤とするビニルエーテル類のカチオン重合反応の分子量制御、分子量分布制御に、マイクロフローシステムが効果的であることが分かった。また、マイクロフローシステムは、より実用性の高いトリフルオロメタンスルフォン酸を開始剤とする重合反応の制御にも有効であることを明らかにした。さらに、連結型マイクロフローシステムを用いてアリルトリメチルシランや異なるモノマーをポリマー成長末端に対して導入することにより、末端官能基化やブロックコポリマーの合成が可能であることも分かった。

Before using the microflow system, the reaction using a conventional macrobatch reactor was examined. A solution of vinyl monomer (5 mL, 2.5 M in CH_2Cl_2) was added dropwise to a solution of **2** (5 mL, 0.05 M in CH_2Cl_2) in a glass flask (50 mL) at a regular pace with vigorous magnetic stirring for 1 min at −78 °C. Immediately after mixing, the reaction mixture was quenched by $i\mathrm{Pr_2NH/CH_2Cl_2}$ (0.83 M, 3 mL) at the same temperature, to give the polymer in quantitative yield. The polymerization reactions of *n*-butyl vinyl ether (NBVE), *iso*-butyl vinyl ether (IBVE), *tert*-butyl vinyl ether (TBVE), styrene, *p*-methoxystyrene, and *N*-vinylcarbazole proceeded smoothly to give the corresponding polymers, but the molecular weight distribution was not narrow as shown in Table 1.

Table 1. Cationic polymerization of monomers initiated by an *N*-acyliminium ion pool (**2**) using a batch reactor.

Monomer	Yield [%]	M_n[a]	M_w/M_n[a]
NBVE	100	5700	2.56
IBVE	100	6900	4.31
TBVE	100	7100	2.29
styrene	100	13000	2.45
p-methoxystyrene	85	560000	2.47
N-vinylcarbazole	84	65000	4.50

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

The effect of the mixing method on the molecular weight (M_n) and molecular weight distribution (M_w/M_n) control was examined for NBVE. As shown in Table 2, the addition of NBVE (5 mL, 2.5 M in CH_2Cl_2, 5 mL min^{-1}) to a solution of **2** (5 mL, 0.05 M in CH_2Cl_2) in a glass flask (50 mL) gave the polymer in a quantitative yield after quenching with $i\mathrm{Pr_2NH/CH_2Cl_2}$, but the molecular weight distribution was not narrow ($M_n = 5700$, $M_w/M_n = 2.56$). The reverse addition gave rise to a similar molecular weight distribution (quantitative yield, $M_n = 24500$, $M_w/M_n = 2.43$). The simultaneous addition of NBVE and **2** did not improve the molecular weight distribution control (quantitative yield, $M_n = 13100$, $M_w/M_n = 2.25$). However, these results show that the molecular weight strongly depends upon the method of mixing.

Table 2. Examination of mixing methods in cationic polymerization of NBVE by an *N*-acyliminium ion pool (**2**) using a batch reactor.

Mixing method	M_n[a]	M_w/M_n[a]
The addition of NBVE to **2**	5700	2.56
The addition of **2** to NBVE	24500	2.43
The simultaneous addition of **2** and NBVE	13100	2.25

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

Cationic Polymerization of *n*-Butyl Vinyl Ether Initiated by an *N*-Acyliminium Ion Pool using a Microflow System

Experiments in a macrobatch reactor showed that the molecular weight depended strongly on the method of mixing, because the rate of the polymerization is so fast. Thus, we hoped that an extremely fast mixing would enable the control of the molecular weight and its distribution. To examine the effect of extremely fast mixing for polymerization, we employed a microflow system consisting of two micromixers (**M1** and **M2**) and two microtube reactors (**R1** and **R2**), shown in Figure 1. As **M1**, where the "cation pool" and the monomer are mixed, a multilamination-type micromixer (IMM micromixer, channel width: 40 µm) was used.

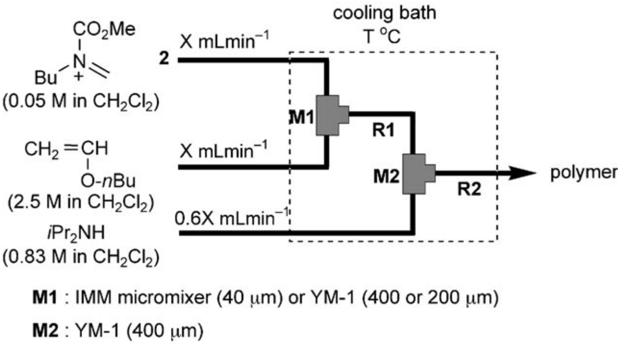


Figure 1. Microflow system for polymerization. **M1** and **M2**: IMM micromixer (40 µm) or YM-1 (400 or 200 µm), **R1** and **R2**: microtube reactor (**R1**: ∅ = 1.0 mm, length = 10 cm, **R2**: ∅ = 1.0 mm, length = 50 cm).

In the IMM mixer, the fluids to be mixed are introduced into the mixing element as two counter-flows and the fluids stream into an interdigital channel (40 µm) configuration. In the next stage, a periodical flow configuration consisting of the lamellae of the two fluids is generated by means of the slit-shaped interdigital channel. Then, the lamellated flow leaves the device perpendicular to the direction of the feed flows.

Thus, solutions of **2** (0.05 M in CH_2Cl_2) and NBVE (2.5 M in CH_2Cl_2) were introduced to **M1** by syringe pumping (flow rate: 5.0 mL min⁻¹) at −78 °C. Then, the reaction mixture was introduced to a microtube reactor (**R1**; ∅ = 1.0 mm, length = 10 cm), in which the polymerization took place. In the final stage, 0.83 M *i*Pr_2NH/CH_2Cl_2 (flow rate: 3 mL min⁻¹) was introduced through **M2** to quench the polymerization. As **M2**, a splitting and recombination-type micromixer, Yamatake YM-1 (400 µm), was used. In the YM-1 micromixer, the two fluids to be mixed are introduced into a segment and combined. Then, the mixture is split into two streams, which are introduced into the next segment.

We found that the polymerization was complete within the residence time of 0.48 s (Table 3). The polymer was obtained in a quantitative yield. More outstanding is the significant improvement of the control of molecular weight distribution (M_n = 6700, M_w/M_n = 1.14). On the other hand, when the YM-1 (400 µm) was used as **M1**, where the "cation pool" and the monomer are mixed, **2** (0.05 M) and NBVE (2.5 M), a polymer with a broad molecular weight distribution (M_n = 8500, M_w/M_n = 1.65) was obtained. The use of a YM-1 (400 µm) as **M1** resulted in a poorer molecular weight distribution control than that using an IMM micromixer, probably because of its lower efficiency of mixing at this flow rate.[11a] However, when YM-1 (200 µm) was used, polymer of a narrower molecular weight distribution (M_n = 6300, M_w/M_n = 1.26) was obtained. These results show the importance of mixing devices. The effect of flow rate on molecular weight distribution also indicates the importance of mixing, because it is well known that mixing efficiency decreases with a decrease in flow rate for the IMM micromixer.[21] Furthermore, M_w/M_n increased with increasing temperature as shown in Table 3. Hence, reaction temperature was also important for controlling the molecular weight distribution.

Table 3. Cationic polymerization of NBVE initiated by *N*-acyliminium ion pool (**2**) using microflow systems (Figure 1).

M1 (micromixer)	X (mL min⁻¹)	T [°C]	M_n[a]	M_w/M_n[a]
IMM micromixer	5	−78	6700	1.14
YM-1(400 µm)	5	−78	8500	1.65
YM-1(200 µm)	5	−78	6300	1.26
IMM micromixer	3	−78	5600	1.35
IMM micromixer	1	−78	6200	2.84
IMM micromixer	5	−48	7300	1.47
IMM micromixer	5	−27	5500	1.34
IMM micromixer	5	0	6500	1.61

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

M_n increased linearly with an increase in monomer/initiator ratio (Figure 2) indicating that transfer reactions did not play significant roles in this system.

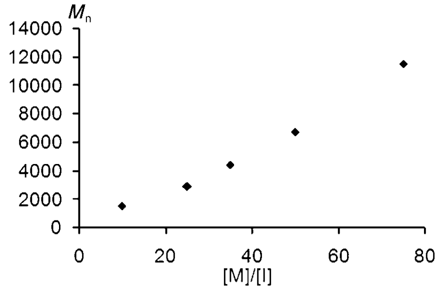


Figure 2. Plots of molecular weight (M_n) against monomer/initiator ratio in cationic polymerization of NBVE initiated by an *N*-acyliminium ion pool (**2**) using a microflow system (Figure 1).

The present results demonstrate that a high level of molecular weight control can be achieved by the control of the initiation process, which is facilitated by fast micromixing. Precise temperature control for the polymerization in the microflow system by virtue of effective heat transfer also seems to be responsible for the remarkable control.

The present method can be applied to other vinyl ethers such as IBVE and TBVE, whereas the corresponding macrobatch reactions for these monomers resulted in a much poorer molecular weight distribution control (Table 4).

Table 4. Cationic polymerization of vinyl ethers (IBVE and TBVE) initiated by an *N*-acyliminium ion pool (**2**) using a microflow system (Figure 1).

Monomer	[M]/[I]	T [°C]	Mixing method	M_n[a]	M_w/M_n[a]
IBVE	50	−78	batch[b]	6900	4.31
			microflow system[c]	7900	1.12
TBVE	50	−78	batch[b]	7100	2.29
			microflow system[c]	7600	1.50

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples. [b] A solution of vinyl monomer (5 mL, 2.5 M in CH_2Cl_2) was added dropwise to a solution of **2** (5 mL, 0.05 M in CH_2Cl_2) in a glass flask (50 mL) at regular pace with vigorous magnetic stirring for 1 min at −78 °C to give the polymer in a quantitative yield after quenching with 0.83 M iPr$_2$NH/CH_2Cl_2. [c] A solution of **2** (0.05 M, 5 mL min^{-1}) and that of a monomer (2.5 M, 5 mL min^{-1}) were introduced to **M1** by syringe pumping (flow rate: 5.0 mL min^{-1}) at −78 °C. Then, the reaction mixture was introduced to a tube reactor (**R1**) (∅ = 1.0 mm, 10 cm). In the final stage, iPr$_2$NH/CH_2Cl_2 (0.83 M, 3 mL min^{-1}) was introduced through Yamatake YM-1 (**M2**) to quench the polymerization. The outlet solution from **R2** (∅ = 1.0 mm, length = 50 cm) was taken into a flask.

It is important to know whether the *N*-acyliminium ion initiating group was really incorporated into the polymer chain. It is also important to know the nature of the polymer end. To examine these factors, the polymerization of NBVE (10 equiv) was carried out with **2** and was quenched by the addition of allyltrimethylsilane (Figure 3).

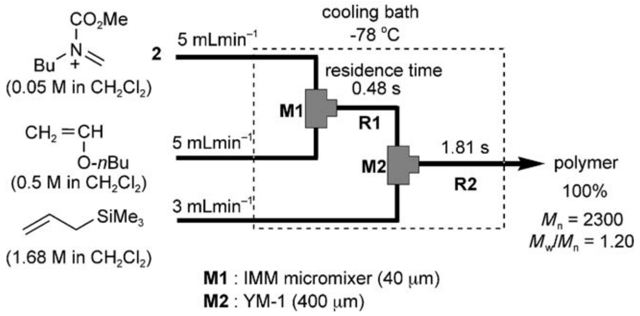


Figure 3. Trapping of polymer end using a microflow system. **M1**: IMM micromixer (40 µm), **M2**: YM-1 (400 µm), **R1** and **R2**: microtube reactor (**R1**: ∅ = 1.0 mm, length = 10 cm, **R2**: ∅ = 1.0 mm, length = 50 cm).

The resulting polymer was analyzed by ^{1}H NMR. As shown in Figure 4, the methoxy group derived from **2** was clearly observed at $\delta = 3.68$ ppm. It is also worth noting that an allyl group was observed as the end group (olefinic protons, $\delta = 5.02$–5.10 and 5.76–5.88 ppm, relative number of protons based on the methoxy group: $\delta = 2.09$ and 1.03 ppm, respectively), indicating that the carbocationic polymer end was trapped by the added allyltrimethylsilane. It is also noteworthy that the relative number of protons adjacent to oxygen in the main chain ($\delta = 3.3$–3.7 ppm) was 48.47 (4 protons adjacent to nitrogen overlapped), indicating that 16.16 of the monomer units were incorporated in a single polymer chain in average. Because 10 equiv of the monomer based on precursor **1** was used for the polymerization, this number is a little large, but cannot be unreasonable if we consider that the efficiency of the conversion of **1** to **2** is 70–80 %. The present observations indicate that the polymer end was really living within the residence time of 0.48 s at −78 °C.

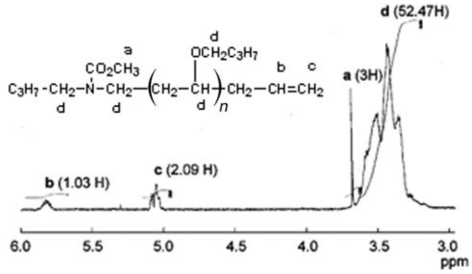


Figure 4. ^{1}H NMR spectrum (600 MHz, in $CDCl_3$) of the polymer obtained by the microflow system controlled polymerization of NBVE, which was initiated by **2** and terminated by allyltrimethylsilane (Figure 3).

Block Copolymerization Initiated by an *N*-Acyliminium Ion Pool using a Microflow System

One of the advantages of living polymerization is that the method allows flexible synthesis of structurally defined block copolymers composed of different monomers, which would offer greater opportunities for the synthesis of organic materials with interesting properties. We hoped that cationic polymerization using a microflow system would offer a simple method for the synthesis of block polymers. Thus, we next examined block copolymerization initiated by a cation pool of **2** using a microflow system (Figure 5). Thus, solu-

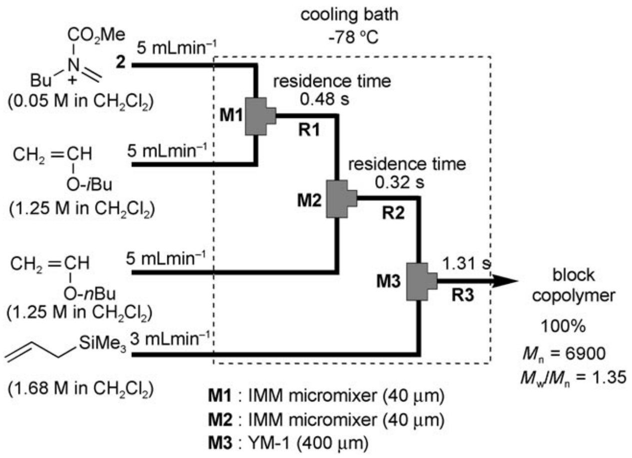


Figure 5. Microflow-system-controlled block polymerization of NBVE and IBVE, which was initiated by **2** and terminated by allyltrimethylsilane. **M1**, **M2** and **M3**: IMM micromixer (40 µm) or YM-1 (400 µm), **R1**, **R2** and **R3**: microtube reactor (**R1**: ∅ = 1.0 mm, length = 10 cm, **R2**: ∅ = 1.0 mm, length = 10 cm, **R3**: ∅ = 1.0 mm, length = 50 cm).

tions of **2** (0.05 M) and IBVE (1.25 M) in CH_2Cl_2 were introduced to an IMM micromixer (**M1**) by syringe pumping (flow rate: 5.0 mL min^{-1}) at −78 °C. Then, the reaction mixture was introduced to a microtube reactor (**R1**; $\varnothing$ = 1.0 mm, length = 10 cm), in which the first polymerization took place. In the next stage, a solution of NBVE (1.25 M) in CH_2Cl_2 was introduced to an IMM micromixer (**M2**) by syringe pumping (flow rate: 5.0 mL min^{-1}). The reaction mixture was introduced to a microtube reactor (**R2**; $\varnothing$ = 1.0 mm, length = 10 cm), in which the second polymerization took place. In the final stage, allyltrimethylsilane was introduced through a Yamatake YM-1 (**M3**) to quench the polymerization. The sequential polymerization took place quite effectively (100 % yield) with good control of the molecular weight distribution ($M_n = 6900$, $M_w/M_n = 1.35$) (Figure 5). The introduction of the second monomer (NBVE, 25 equiv based on the cation pool initiator) resulted in the formation of a polymer of higher molecular weight ($M_n = 6900$), whereas the polymer obtained by polymerization of 25 equivalents of NBVE based on the cation pool initiator followed by quenching with $i\text{Pr}_2\text{NH}/CH_2Cl_2$ gave $M_n = 2900$ (Figure 6). These results show that microflow-system-controlled polymerization using a cation pool as an initiator is effective for the synthesis of a block polymer.

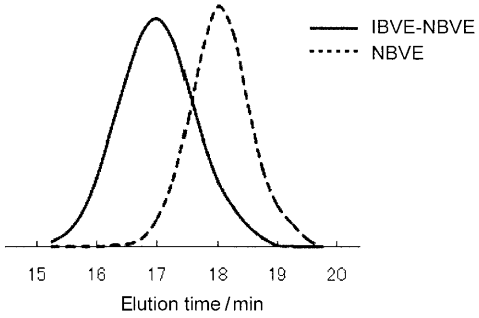


Figure 6. GPC traces of copolymerization with different monomers.

Cationic Polymerization Initiated by Trifluoromethanesulfonic Acid (TfOH) using a Macrobatch Reactor

Generation of a cation pool initiator needs electrochemical oxidation at low temperature. This might be a major drawback from a viewpoint of practical polymer synthesis. Thus, we examined proton-initiated polymerization in a microflow system, because various Brønsted acids are commercially available. As a Brønsted acid initiator, we decided to focus on trifluoromethanesulfonic acid (TfOH)[22] after several trials with other acids.

Before using a microflow system, the reaction using a conventional macrobatch reactor was examined. To a solution of NBVE in 1,2-dicholoroethane (25 mL) at −25 °C or −78 °C, TfOH (1.0 mL) was added for 1 min with vigorous magnetic stirring. After stirring for 10 s, the reaction was quenched with diisopropylamine in methanol (5 mL). The polymerization was complete within 10 s even at −78 °C, and the polymer was obtained in a quantitative yield. The molecular weight increased with an increase in the monomer/initiator ratio but the molecular weight distribution of the polymer became broader as the monomer concentration increased, probably because of greater heat generation per unit volume (Table 5). The molecular weight distribution was much broader at −25 °C ranging from 2.80 to 4.61 as shown in Table 5, indicating that the polymerization is too fast to control using a conventional macrobatch reactor.

Table 5. TfOH initiated polymerization of NBVE in a batch reactor.

T [°C]	[M]/[I]	M_n[a]	M_w/M_n[a]
−78	50	5500	1.39
−78	75	7600	1.47
−78	100	9500	1.78
−78	125	10800	2.03
−78	150	12900	2.42
−25	50	3300	2.80
−25	75	3400	2.88
−25	100	3700	3.05
−25	125	4700	3.76
−25	150	5100	4.61

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

Cationic Polymerization Initiated by Trifluoromethanesulfonic Acid (TfOH) using a Microflow System

The TfOH-initiated polymerization in a microflow system was examined. A microflow system consisting of two IMM micromixers (**M1** and **M2**, channel width: 40 μm) and two microtube reactors (**R1** and **R2**, $\varnothing$ = 500 μm, length = 25 cm) was used (Figure 7). A monomer solution (0.5 M) and an initiator solution (0.01 M) in 1,2-dichloroethane were introduced to **M1** by syringe pumping. A solution of $i\text{Pr}_2\text{NH}$ in MeOH was introduced to **M2** to quench the polymerization. The polymer was obtained in a quantitative yield. The high level of molecular distribution control was attained even at −25 °C as shown in Table 6. It is important to note that very low temperatures such as −78 °C, which might be an obstacle to industrial-scale applications,[23] are not re-

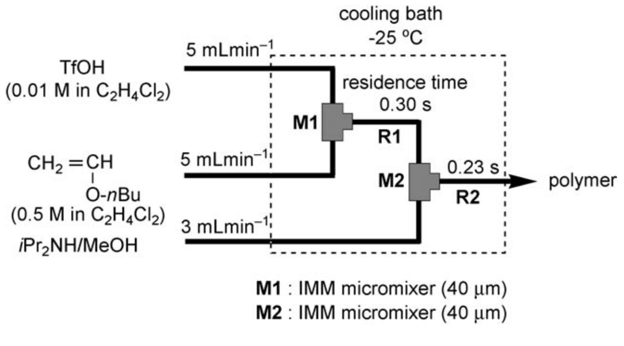


Figure 7. Microflow system for polymerization. **M1** and **M2**: IMM micromixer (40 μm), **R1** and **R2**: microtube reactor ($\varnothing$ = 500 μm, length = 25 cm).

Table 6. TfOH-initiated polymerization of NBVE in microflow system at various monomer/initiator ratio (Figure 6).

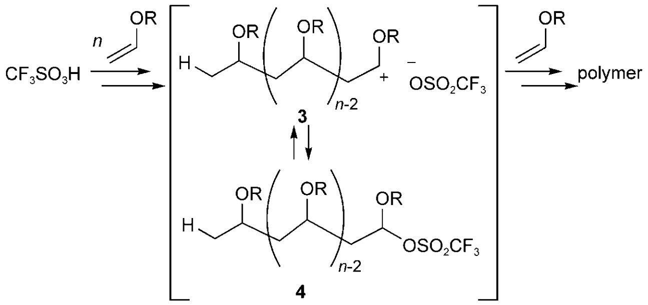
T [°C]	[M]/[I]	M_n[a]	M_w/M_n[a]
−25	10	2200	1.24
−25	25	3500	1.33
−25	40	5100	1.33
−25	50	6900	1.38
−25	75	9800	1.49

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

quired to attain a high degree of molecular weight distribution control in the present system.

M_n increased with an increase in the monomer/initiator ratio. The results indicate that transfer reactions did not play significant roles in the present system, which is consistent with the observed high level of molecular weight distribution control.

Although the details are not clear at present, the successful control of molecular weight distribution at higher temperatures can be ascribed to the stability of 1-(alkoxy)alkyl triflate intermediate (**4**), which might exist as an equilibrium mixture with a 1-(alkoxy)carbenium ion intermediate (**3**)[24] in the propagation step (Scheme 2). Although there is no experimental evidence for the formation of **4**,[25] it is noteworthy that glycosyl triflates have been known to exist as well-characterized intermediates in glycosylation reactions.[26]



Scheme 2. Equilibrium mixture with an 1-(alkoxy)carbenium ion intermediate.

DFT calculations in the gas phase indicated that the covalent bond formation between alkoxycarbenium ion **5** and triflate anion **6** to give (1-alkoxy)alkyltriflate **7** (Figure 8) is highly exoergonic (−118.8 kcal mol^{-1}), although the ion pair of **5** and **6** should be significantly stabilized by solvation in the solution phase.

Next, we studied on the microflow systems using T-shaped micromixers to develop more practically useful systems for controlled cationic polymerization. The simple T-junction structures of T-shaped micromixers are much simpler than those of multilamination-type micromixers and splitting and recombination-type micromixers. Therefore, T-shaped micromixers are expected to serve as practical systems for continuous operation without clogging and a high pressure drop.[23a] Easy fabrication and low costs are also advantages of T-shaped micromixers. A microflow system consisting of a T-shaped micromixer (**M1**, ∅ = 250 μm) and a microtube reactor (**R1**, ∅ = 500 μm, length = 50 cm; Figure 9) was found to be quite effective for the polymerization as shown in Table 7. The polymerization was complete within the residence time of 0.37–1.5 s, and the polymer was obtained in almost quantitative yield.

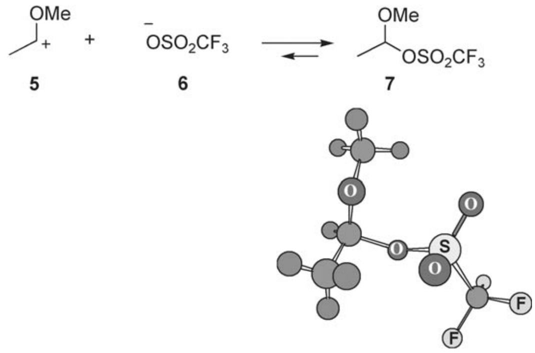


Figure 8. Optimized structure of triflate **7** obtained by DFT calculation (B3LYP/6-31G(d)). C-OTf: 1.504 A.

High level of molecular distribution control similar to the case with the multilamination-type micromixer was attained with a T-shaped micromixer of 250 μm diameter, although the M_w/M_n increased with a decrease in the flow rate (< 5 mL min^{-1}) and with an increase in the inner diameter of

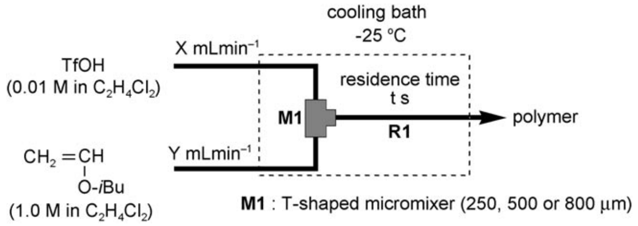


Figure 9. Microflow system based on the T-shaped micromixer for polymerization. **M1**: T-shaped micromixer (250, 500 or 800 μm), **R1**: a microtube reactor (∅ = 500 μm, length = 50 cm).

Table 7. TfOH initiated polymerization of IBVE in microflow systems (Figure 8).

M1 Diameter [μm]	X [mL min^{-1}]	Y [mL min^{-1}]	t [s]	M_n[a]	M_w/M_n[a]
250	2	2	1.50	2900	2.30
250	3	3	0.98	1600	1.61
250	4	4	0.74	5100	1.33
250	5	5	0.59	1500	1.22
250	6	6	0.49	1500	1.22
250	7	7	0.42	1500	1.19
250	8	8	0.37	1500	1.22
500	5	5	0.59	2000	2.54
500	6	6	0.49	1500	1.82
500	7	7	0.42	1400	1.67
800	6	6	0.49	2300	2.89

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

the micromixer (Table 7). It is important to note that a stable continuous operation with a low pressure drop was attained, presumably by virtue of the simple inner structures of the T-shaped micromixer.

As shown in Figure 10, M_n increased with an increase in the monomer/initiator ratio. These results also indicate that transfer reactions did not play significant roles in the present system, which is consistent with the observed high level of molecular weight distribution control. The polymerization of other vinyl ether monomers such as NBVE and ethyl vinyl ether (EVE) also took place in highly controlled manners. The molecular weight increased with an increase in the monomer/initiator ratio as shown in Figure 11.

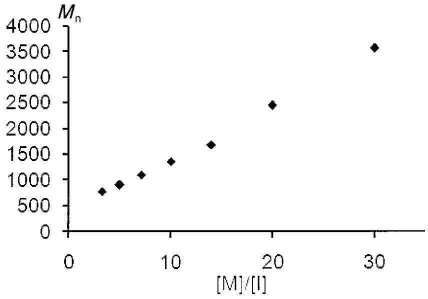


Figure 10. Plots of molecular weight (M_n) against monomer/initiator ratio in the cationic polymerization of IBVE initiated by TfOH using a microflow system (Figure 9).

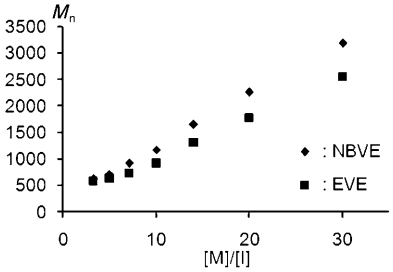


Figure 11. Plots of molecular weight (M_n) against monomer/initiator ratio in the cationic polymerization of NBVE and EVE initiated by TfOH using a microflow system (Figure 9).

In order to get a better insight into the nature of the polymer end, the polymerization was quenched by the addition of allyltrimethylsilane. Thus, the polymerization of IBVE was carried out with 0.1 equiv of CF_3SO_3H using the microflow systems shown in Figure 12, and allyltrimethylsilane was introduced using the second T-shaped micromixer (**M2**, $\varnothing = 250\ \mu m$). The ^1H NMR analysis of the resulting polymer ($M_n = 1200$, $M_w/M_n = 1.36$) revealed that an allyl group was introduced as the end group (olefinic protons, $\delta = 5.0$–5.10 and 5.7–5.9 ppm, Figure 13). The present observation indicates that the carbocationic polymer end was effectively trapped by the added allyltrimethylsilane. The polymer end was really living in the microtube reactor within the residence time of 0.59 s.

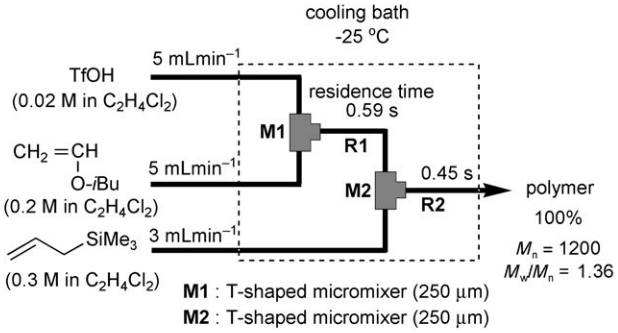


Figure 12. A schematic diagram of the microflow system based on the T-shaped micromixer for polymerization and termination with allyltrimethylsilane. **M1** and **M2**: T-shaped micromixer (250 µm), **R1** and **R2**: microtube reactor (**R1**: $\varnothing = 500\ \mu m$, length = 50 cm, **R2**: $\varnothing = 500\ \mu m$, length = 50 cm).

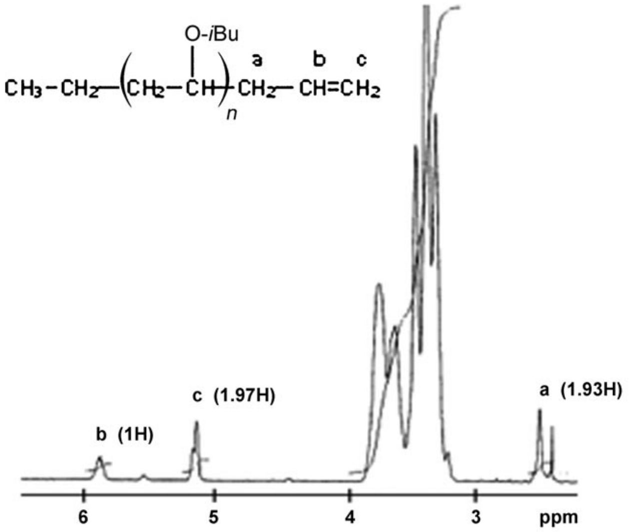


Figure 13. 600 MHz ^1H NMR spectrum of the polymer obtained by the quenching with allyltrimethylsilane.

Block Copolymerization using a Microflow System

Block copolymerization was examined using a microflow system consisting of two T-shaped micromixers and two microtube reactors (Figure 14). The polymerization of vinyl ether (IBVE, NBVE or EVE, 10 equiv based on TfOH initiator) followed by MeOH quenching at the second micromixer (**M2**) gave the homopolymer (Table 8). The introduction of the second monomer (IBVE, NBVE or EVE, 10 equiv based on TfOH initiator) at the second micromixer (**M2**) resulted in the formation of the polymer of higher molecular weight with narrow molecular weight distribution as shown in Table 8 and Figure 15.

Block copolymerization could be carried out with any combination and with either order of monomer addition as shown in Table 8, demonstrating that the present microflow system serves as an effective tool for the synthesis of block copolymers.

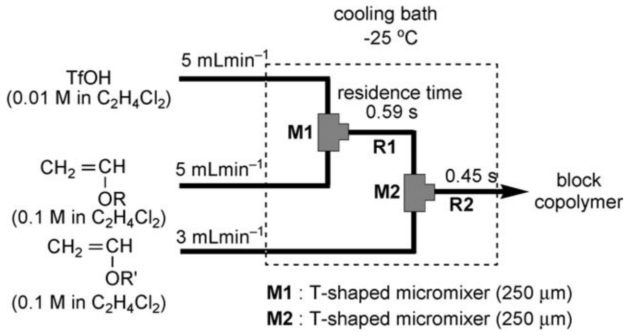


Figure 14. A schematic diagram of the microflow system based on the T-shaped micromixer for block copolymerization. **M1** and **M2**: T-shape micromixer (250 µm), **R1** and **R2**: microtube reactor (**R1**: ∅ = 500 µm, length = 50 cm, **R2**: ∅ = 500 µm, length = 50 cm).

Table 8. Block copolymerization using microflow system.

Monomer-1	Monomer-2	M_n[a]	M_w/M_n[a]
IBVE	–	1400	1.18
IBVE	NBVE	2300	1.43
IBVE	EVE	1800	1.54
NBVE	–	1000	1.24
NBVE	IBVE	1700	1.45
NBVE	EVE	1900	1.55
EVE	–	860	1.16
EVE	IBVE	2100	1.54
EVE	NBVE	2100	1.41

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

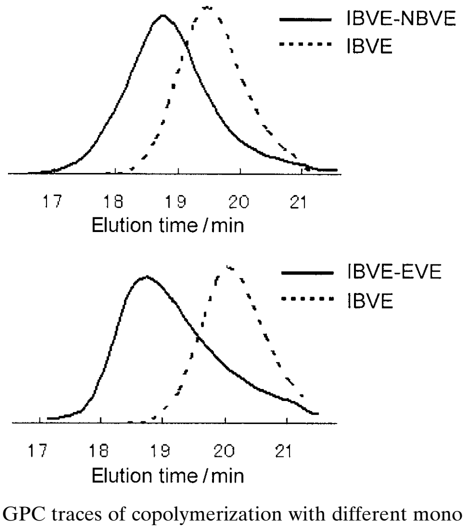


Figure 15. GPC traces of copolymerization with different monomers.

Microflow-System-Controlled Polymerization at Higher Concentrations using a Halogen Free Solvent

Since 1,2-dichloroethane is not a suitable solvent for industrial polymerization because of its toxicity, we searched for halogen-free organic solvents for the present TfOH-initiated microflow-system-controlled carbocationic polymerization. Eventually, toluene was found to serve as a good alternative. It is important to conduct the polymerization at higher concentration from the viewpoint of industrial applications, because productivity increases with an increase in the concentration of a monomer. Thus, the concentration of the monomer solution and that of the initiator solution were increased to 2.5 M and 0.25 M, respectively. As shown in Table 9, the polymerization in toluene may be conducted at higher concentrations without any problem, although the level of molecular weight distribution control was slightly lower. It should be noted that the present laboratory scale system has the productivity of 45–105 g h^{-1} of the polymer, suggesting that the microflow-system-controlled carbocationic polymerization can be applicable to industrial production by further scaling-up of a single flow system and its numbering-up.

Table 9. Polymerization of IBVE at higher concentration using toluene as solvent.

M1 Diameter [µm]	X [mL min^{-1}]	Y [mL min^{-1}]	[M]/[I]	M_n[a]	M_w/M_n[a]
250	3	9	3.3	930	1.23
250	4	8	5	1000	1.23
250	5	7	7.1	1200	1.26
250	6	6	10	1300	1.29
250	7	5	14	1400	1.31
250	8	4	20	2000	1.10
250	9	3	30	2600	1.28

[a] Polymers were analyzed with size exclusion chromatography with the calibration using standard polystyrene samples.

Conclusions

In conclusion, microflow-system-controlled carbocationic polymerization of vinyl ethers has been achieved by using a "cation pool" as an initiator at −78 °C. The molecular weight distribution can be controlled by extremely fast micromixing using a multilamination-type micromixer, and the polymer end can be used as living reactive species for the subsequent reaction, such as a trapping reaction by a nucleophile. Block copolymerization using two different monomers could also be achieved. The polymerization was also conducted using commercially available trifluoromethanesulfonic acid (TfOH) as an initiator. In this case, a high level of molecular weight distribution control was achieved even at −25 °C. In addition, the cationic polymerization of vinyl ethers was conducted by using a microflow system consisting of T-shaped micromixers instead of expensive multilamination micromixers. Block copolymerization of two different monomers was also achieved using the system. Toluene may be used as a halogen free solvent, which is more suitable for an industrial application. In this solvent, the polymerization could be conducted at high concentrations of monomer and initiator without any problem. The observations illustrated here increase the possibility of microflow-system-controlled polymerization for practical synthesis of structurally well-defined polymers and copolymers. It is hoped that the method will be applied for industrial production of polymers based on a numbering-up technology in the future.

Experimental Section

Typical Procedure for Cationic Polymerization Using a Cation Pool in a Microflow System

A microflow system consisting of two micromixers (**M1** and **M2**) and two tube reactors (**R1** and **R2**) was used. Pre-cooling units ($\varnothing = 1000\,\mu\mathrm{m}$, length $= 100$ cm) were connected to an inlet of the micromixers **M1** and **M2**. The whole system was cooled in a dry ice/hexane bath at $-78\,^{\circ}\mathrm{C}$. As **M1**, where the cation pool and a monomer are mixed, an IMM micromixer was used. Solutions of **2** in dichloromethane (0.05 M, 5.0 mL min^{-1}) and a monomer (0.5–2.5 M, 5.0 mL min^{-1}) were introduced to **M1** through the pre-cooling unit by syringe pumping at $-78\,^{\circ}\mathrm{C}$. Then, the reaction mixture was introduced to a microtube reactor (**R1**; $\varnothing = 1.0$ mm, 10 cm), in which the polymerization took place. In the final stage, $i\mathrm{Pr_2NH/CH_2Cl_2}$ (0.83 M, 3 mL min^{-1}) was introduced through **M2** to quench the polymerization in **R2** ($\varnothing = 1.0$ mm, length $= 50$ cm). As **M2**, a Yamatake YM-1 was used. The outlet solution from **R2** was collected in a flask. The mixture was warmed to room temperature after quenching. The solvent was removed under reduced pressure and the residue was filtered through a column (15 cm) of silica gel with $\mathrm{Et_2O}$ elution (180 mL) to remove $\mathrm{Bu_4NBF_4}$. The solution was concentrated to obtain a polymer product in a quantitative yield.

Typical Procedure for Cationic Polymerization Using TfOH in a Microflow System Based on a T-shaped Micromixer

A microflow system consisting of a T-shaped micromixer **M1** (inner diameter: 250 μm) and a microtube reactor **R1** (inner diameter: 500 μm, length: 50 cm) was used. Pre-cooling units ($\varnothing = 1000\,\mu\mathrm{m}$, length $=$ 100 cm) were connected to an inlet of the micromixer **M1**. The whole system was cooled in a cooling bath at $-25\,^{\circ}\mathrm{C}$. Solution of IBVE in 1,2-dichloroethane (0.2 M, 6.0 mL min^{-1}) and that of TfOH in 1,2-dichloroethane (0.02 M, 6.0 mL min^{-1}) were introduced to **M1** through the pre-cooling unit by syringe pumping at $-25\,^{\circ}\mathrm{C}$. The outlet solution from the **R1** was introduced to a solution of saturated potassium carbonate in methanol to quench the polymerization. GC analysis of the obtained solution revealed the absence of any of the starting monomer. The resulting mixture was poured into water. The organic phase was separated and the aqueous phase was extracted with hexane or tetrahydrofuran. The combined organic phase was dried over sodium carbonate. After filtration, the solvent was removed under reduced pressure to obtain the polymer product.

Acknowledgements

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