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Polymerization of Vinyl Ethers Initiated by Dendritic Cations Using Flow Microreactors

Aiichiro Nagaki, Masahiro Takumi, Yosuke Tani, and Jun-ichī Yoshida*
Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan.
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a Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan.

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∗ Corresponding author. Tel.: +81-75-383-2726; fax: +81-75-383-2727; e-mail: yoshida@sbchem.kyoto-u.ac.jp

1. Introduction

Linear-dendritic polymers have emerged as a new important type of macromolecules in materials science, and the ambivalent characteristics of their architecture offer unique/new possibilities for numerous potential applications. Linear-dendritic polymers can be prepared based on three strategies: (1) coupling strategy, (2) chain-first strategy, and (3) dendron-first strategy. Especially the dendron-first approach is very useful because the dendrimers can be constructed by a convergent synthetic route such as coupling of prefabricated branched units.

We have developed the cation pool method in which organic cations are electrochemically generated and accumulated in solution in the absence of nucleophiles and are used for the reactions with subsequently added nucleophiles. The method has been successfully applied to various organic cations including $N$-acyliminium ions, alkoxy carbocation ions, and diarylcarbenium ions. We have also developed an iterative process for making dendritic structures based on the cation pool method; a sequence consisting of the electrochemical generation of a diarylcarbenium ion (activation) followed by the reaction with (diphenylmethyl)trimethylsilane as a building block (coupling) is repeated to effect convergent synthesis of dendritic molecules (Figure 1). Notably, dendritic diarylcarbenium ions react with unfunctionalized polystyrenes to give dendronized polymers.
Chemical synthesis in flow microreactors has attracted a great deal of attention and the applications to polymerization of vinyl monomers have been extensively studied. For example, controlled cationic polymerization of vinyl ethers and controlled anionic polymerization of styrenes, alkyl methacrylates, and tert-butyl acrylate using flow microreactors have been reported in the literature. The molecular weight and the molecular weight distribution can be strictly controlled by virtue of the characteristic features of flow microreactors such as fast mixing, fast heat transfer, and precise residence time control.

Based on these achievements, the following working hypothesis came to our mind. Use of dendritic diarylcarbenium ions as initiators of controlled cationic polymerization in flow microreactors leads to the formation of linear-dendritic polymers bearing living polymer ends which can be trapped with nucleophiles (dendron-first strategy). The method would serve as a powerful and straightforward way of synthesizing structurally well-defined linear-dendritic polymers. However, to the best of our knowledge, such an approach has not yet been reported so far, which has a silyl group as an electroauxiliary for the selective functionalization (Figure 2).

**Figure 2.** Generation of diarylcarbenium ion 2.

First, we examined the polymerization of isobutyl vinyl ether using diarylcarbenium ion 2 in a flow microreactor system composed of two T-shaped micromixers (M1 and M2) and two microtube reactors (R1 and R2) (Figure 3). The flow microreactor system was dipped in a cooling bath (-78 °C). A solution of isobutyl vinyl ether (0.50 M in CH2Cl2, 10 mL/min) and a solution of 2 (0.050 M in CH2Cl2, 5 mL/min) were mixed using M1 (φ = 250 μm). The mixed solution was introduced to R1 (φ = 1000 μm, L = 25 cm), where the polymerization took place. The polymerization was terminated by adding a solution of trimethyl(1-phenylvinylxoy)silane (1.0 M in CH2Cl2, 5 mL/min) at M2 (φ = 500 μm) and R2 (φ = 1000 μm, L = 50 cm) to obtain the end-functionalized polymer 3. When the polymerization was carried out in the presence of a proton trapping agent, the agent was added to a solution of 2 prior to the polymerization.

### Table 1. Cationic polymerization of isobutyl vinyl ether initiated by diarylcarbenium ion 2 in the absence or presence of a proton trapping agent using a flow microreactor system.

<table>
<thead>
<tr>
<th>Proton Trapping Agent</th>
<th>Mn (× 10^3)</th>
<th>Mw/Mn</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>5200</td>
<td>1.08</td>
<td>61</td>
</tr>
<tr>
<td>tert-Butylpyridine</td>
<td>13400</td>
<td>1.10</td>
<td>66</td>
</tr>
<tr>
<td>2,6-di-tert-Butylpyridine</td>
<td>12100</td>
<td>1.19</td>
<td>83</td>
</tr>
<tr>
<td>tert-Butylpyridine</td>
<td>16100</td>
<td>1.11</td>
<td>87</td>
</tr>
<tr>
<td>2,6-di-tert-Butylpyridine</td>
<td>1600</td>
<td>1.05</td>
<td>65</td>
</tr>
<tr>
<td>tert-Butylpyridine</td>
<td>9000</td>
<td>1.05</td>
<td>90</td>
</tr>
</tbody>
</table>

Notably, the use of 2,6-di-tert-butylpyridine as a proton trapping agent resulted in a dramatic decrease in the amount of the polymer formed by the proton initiation, although the yield of the polymer was not decreased significantly (Figure 4 (b)). The result indicates that protons, which were presumably generated by the electrolysis, were effectively trapped with 2,6-di-tert-butylpyridine. Therefore, the desired polymer 3 with narrow molecular weight distribution (Mw/Mn = 1.05) was obtained, indicating that diarylcarbenium ion 2 worked well as an initiator. In contrast, the polymerization in the presence of 2,6-di-tert-butylpyridine (0.5 eq) using a batch macro reactor was examined. The addition of 2 (0.050 M in CH2Cl2) and 2,6-di-tert-butylpyridine (0.025 M in CH2Cl2) (5 mL, 5.0 mL/min) to a solution of isobutyl vinyl ether (10 mL, 0.50 M in CH2Cl2) in a glass flask (25 mL) gave the polymer in 84% yield after quenching with trimethyl(1-phenylvinylxoy)silane (1.0 M, 1.0 M in CH2Cl2), but the molecular weight distribution was not...
narrow (Mn = 26600, Mw/Mn = 1.45). The reverse addition gave rise to only a slight improvement of the similar molecular weight distribution control (97% yield, Mn = 7560, Mw/Mn = 1.29). The simultaneous addition did not work (96% yield, Mn = 11200, Mw/Mn = 1.59). Thus, it is reasonable to consider that the characteristic features of a flow microreactor system such as fast mixing enables the diarylcarbenium ion initiated polymerization in a highly controlled manner.

The results indicate that extremely fast mixing is responsible initiated by diarylcarbenium ion for narrow molecular weight distribution (Mw/Mn < 1.10). The effective method for synthesis of end functionalized linear-dendritic polymers.

Figure 4. MALDI-TOF mass spectra of the polymers obtained by (a) the polymerization in the absence of a proton trapping agent and (b) the polymerization in the presence of 2,6-di-tert-butylpyridine (0.5 eq).

Next, the effect of mixing was examined. Generally, the mixing speed depends on the flow rate and the inner diameter of a micromixer. As shown in Table 2, the molecular weight distribution strongly depends on the flow rate and the inner diameter of micromixer M1. The polydispersity index (Mw/Mn) decreased with the increase in the total flow rate in M1. The Mw/Mn also decreased with a decrease in the inner diameter of M1. The results indicate that extremely fast mixing is responsible for narrow molecular weight distribution (Mw/Mn < 1.10).

Table 2. Effect of mixing for cationic polymerization of isobutyl vinyl ether in the presence of 2,6-di-tert-butylpyridine (0.5 eq) initiated by diarylcarbenium ion 2 using a flow microreactor.

<table>
<thead>
<tr>
<th>Inner diameter of M1 (µm)</th>
<th>Total flow rate in M1 (mL/min)</th>
<th>Mw/Mn</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>3.0</td>
<td>8600</td>
<td>2'03</td>
</tr>
<tr>
<td>250</td>
<td>9.0</td>
<td>7000</td>
<td>1'11</td>
</tr>
<tr>
<td>250</td>
<td>15.0</td>
<td>8100</td>
<td>1'05</td>
</tr>
<tr>
<td>500</td>
<td>15.0</td>
<td>6100</td>
<td>1'16</td>
</tr>
</tbody>
</table>

*Polymers were analyzed with size exclusion chromatography calibrated with poly styrene.*

In addition to trimethyl(1-phenylvinyloxy)silane, allyltrimethysilane was also used as a terminating agent to obtain the end-functionalized polymer 4 in a good yield with narrow molecular weight distribution (Mw/Mn = 1.06). The 1H NMR spectra of polymers 3 and 4 are shown in Figure 5. The two methine protons (H') derived from 2 was clearly observed at δ = 5.37 ppm (d, J = 2.8 Hz) for 3 and 4). The end group such as an aryl group (for 3: aromatic protons, δ = 7.45, 7.55 and 7.96 ppm), as an allyl group (for 4: olefinic protons, δ = 5.01-5.06 and 5.78-5.84 ppm) were observed. The relative intensities of these protons based on the methine proton (H') indicate that the carbocationic polymer end was effectively trapped by the added nucleophiles. Therefore, the present method serves as an effective method for synthesis of end functionalized linear-dendritic polymers.

Figure 5. 1H NMR spectra of end-functionalized linear-dendritic polymers; (a) 3 and (b) 4.

Cationic Block Copolymerization of Vinyl Ethers Initiated by a Diarylcarbenium Ion Pool Using an Integrated Flow Microreactor System

Next, the block copolymerization of isobutyl vinyl ether and n-butyl vinyl ether was carried out using an integrated flow microreactor systems consisting of three micromixers (M1, M2, and M3) and three microtube reactors (R1, R2, and R3) shown in Figure 6. A solution of 2 (0.050 M) and 2,6-di-tert-butylpyridine (0.025 M) in CH2Cl2 (5 mL/min) and a solution of isobutyl vinyl ether (0.50 M in CH2Cl2, 10 mL/min) were mixed using M1 (ϕ = 250 µm). The mixed solution was introduced to R1, where the polymerization was carried out. Then, the solution of n-butyl vinyl ether (1.0 M in CH2Cl2, 5 mL/min) was introduced to M2 (ϕ = 500 µm), which was connected to R2 (ϕ = 1000 µm, L = 50
cm (-50 °C) or ϕ = 1000 μm, L = 100 cm (-78 °C)) where the second polymerization took place. The polymerization was terminated by introducing a solution of trimethyl(1-phenylvinylxilosilane (1.0 M in CH2Cl2, 5 mL/min) to M3 (ϕ = 500 μm) and R3 (ϕ = 1000 μm, L = 50 cm). GPC traces of the polymers 5 obtained under various conditions are shown in Figure 7.

Figure 7. Size exclusion chromatography traces of the cationic block copolymerization of isobutyl vinyl ether and n-butyl vinyl ether in the integrated flow microreactor system (a) at -50 °C with varying the residence time in R1 and (b) with the residence time of 0.79 s in R1 with varying the temperature.

The 1H NMR (Figure 8) and MALDI-TOF-MS analyses of the resulting polymer 5 revealed that end functional groups were introduced almost quantitatively (See the Supporting Information for details). Notably, the block copolymer 5 bears the bromo groups at the peripheral of the dendritic part, which can be used for further transformations such as Hartwig-Buchwald amination22.

Figure 8. 1H NMR spectrum of end functionalized block copolymers (5).

3. Conclusion

In conclusion, controlled cationic polymerization of vinyl ethers initiated by a cation pool of a dendritic diarylcarbenium ion was successfully achieved using the flow microreactor system. Extremely fast mixing is responsible for narrow molecular weight distribution and the polymer end can be used as living reactive species for the subsequent reactions with a nucleophiles and block copolymerization. The observations illustrated here open a new possibility in the synthesis of linear-dendritic polymers. Further applications of the present method are under investigation in our laboratory.

4. Experimental section

General

1H and 13C NMR spectra were recorded in CDCl3 on JEOL ECA-600P (1H 600 MHz and 13C 150 MHz). Chemical shifts are recorded using a methine signal of CHCl3 for 1H NMR (7.26 ppm) and 13C NMR (77.0 ppm) unless otherwise noted. MALDI-TOF mass spectra were recorded on Bruker ultraflex. Preparative gel permeation chromatography (GPC) was performed on Japan Analytical Industry LC-918. Dichloromethane was washed with water, distilled from P2O5, redistilled from dried K2CO3 to remove a trace amount of acid, and stored over molecular sieves 4Å. Isobutyl vinyl ether and n-butyl vinyl ether were distilled under reduced pressure from CaH2 twice. BuNBF4 was dried at 25 °C/1 mmHg for 12 hours. I was prepared according to reported procedure19. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. All solutions used for flow reactions were prepared under the argon atmosphere using dry solvents.

Stainless steel (SUS304) T-shaped micromixers with inner diameter of 250 and 500 μm were manufactured by Sanko Seiki Co., Inc. Stainless steel (SUS316) microtube reactors with inner diameter of 1000 μm were purchased from GL Sciences. The micromixers and microtube reactors were connected with stainless steel fittings (GL Sciences, 1/16 OUN). The flow microreactor system was dipped in a cooling bath to control the temperature. The solutions were introduced to the flow microreactor system using Harvard Model 11 syringe pumps equipped with gastight syringes purchased from SGE.

Figure 6. Integrated flow microreactor system for cationic block copolymerization of isobutyl vinyl ether and n-butyl vinyl ether initiated by a diarylcarbenium ion 2 in the presence of 2,6-di-tert-butylpyridine. T-shaped micromixers: M1, M2, and M3. Microtube reactors: R1, R2, and R3.

The Mn increased when the second monomer solution was added at -50 °C as shown in Figure 7 (a), indicating that the polymerization of the second monomer took place. However, the bimodal molecular weight distribution even with short residence times in R1 indicates decomposition of the reactive polymer chain end generated by the first polymerization. However, the block copolymerization was successfully carried out without significant decomposition of the living polymer end at -78 °C with a short residence time in R1 (0.79 s) to obtain 5 in 95% yield with narrow molecular weight distribution (Mw/Mn = 1.08) as shown in Figure 7 (b).
Molecular Weight and Molecular Weight Distribution

The molecular weight (Mn) and molecular weight distribution (Mw/Mn) were determined in THF at 40 °C with a Shodex GPC-101 equipped with two LF-804L columns (Shodex) and an RI detector using a Polystyrene (PolySt) standard sample for calibration.

Electrochemical Generation of the Cation Pool from 1

The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 °C /1 mmHg for 2.5 h before use) and a platinum plate cathode (20 mm x 10 mm). A 0.3 M solution of Bu$_4$NBF$_4$/CH$_2$Cl$_2$ (35 mL) was placed in the anodic chamber, and a 0.3 M solution of Bu$_4$NBF$_4$/CH$_2$Cl$_2$ (35 mL) and trifluoromethanesulfonic acid (230 µL, 2.60 mmol) was placed in the cathodic chamber. The constant current electrolysis (40 mA) was carried out at -78 °C with magnetic stirring until 2.0 F/mol of electricity was consumed.

Cationic Polymerization of Isobutyl Vinyl Ether Using Trimethyl(1-phenylvinyloxy)silane as a Terminating Agent in a Flow Microreactor System

After electrolysis the resulting solution of 2 (6 mL, -78 °C) was transferred to a 20 mL flask at -78 °C, and a proton trapping agent was added. The resulting solution was stirred for 10 min at -78 °C. A flow microreactor system consisting of two T-shaped micromixers (M1 and M2), two microtube reactors (R1 and R2), and three pre-cooling units (P1 (inner diameter φ = 1000 µm, length L = 25 cm), P2 (φ = 1000 µm, L = 50 cm), and P3 (φ = 1000 µm, L = 50 cm)) was used for polymerization. A solution of isobutyl vinyl ether (0.50 M in CH$_2$Cl$_2$) and a solution of 1 (0.50 M in CH$_2$Cl$_2$, 5 mL/min) were introduced to M2 (φ = 500 µm). A solution of trimethyl(1-phenylvinyloxy)silane (1.0 M in CH$_2$Cl$_2$, 5 mL/min) was introduced to M3 (φ = 500 µm), and the resulting solution was passed through R3 (φ = 1000 µm, L = 50 cm). After a steady state was reached, the product solution was collected (10 s) and treated with Pr$_2$NH. The reactions were carried out by changing temperature and the residence time in R2 and R3. The solvent was removed under reduced pressure and the residue was filtered through a silica gel column (2 x 3 cm) using Et$_2$O as an eluent to remove Bu$_4$NBF$_4$. The filtrate was concentrated to obtain a polymer product, which was analyzed with size exclusion chromatography. The polymer product was purified with preparative GPC to obtain 5.

Supplementary data

Supplementary data related to this article can be found, in the online version, at http://dx.doi.org/

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References and notes
