

Article

Synthesis of Well-Defined, Water-Soluble Hyperbranched Polyamides by Chain-Growth Condensation Polymerization of AB₂ Monomer

Yoshihiro Ohta¹, Yusuke Kamijyo¹, Akihiro Yokoyama² and Tsutomu Yokozawa^{1,*}

¹ Department of Material and Life Chemistry, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221-8686, Japan; E-Mails: y-ohta0112@kanagawa-u.ac.jp (Y.O.); m20120229@gmail.com (Y.K.)

² Department of Material and Life Science, Seikei University, Kichijoji-Kitamachi, Musashino-shi, Tokyo 180-8633, Japan; E-Mail: ayokoyama@st.seikei.ac.jp

* Author to whom correspondence should be addressed; E-Mail: yokozt01@kanagawa-u.ac.jp; Tel.: +81-45-481-5661; Fax: +81-45-413-9770.

Received: 12 March 2012; in revised form: 18 April 2012 / Accepted: 8 May 2012 /

Published: 14 May 2012

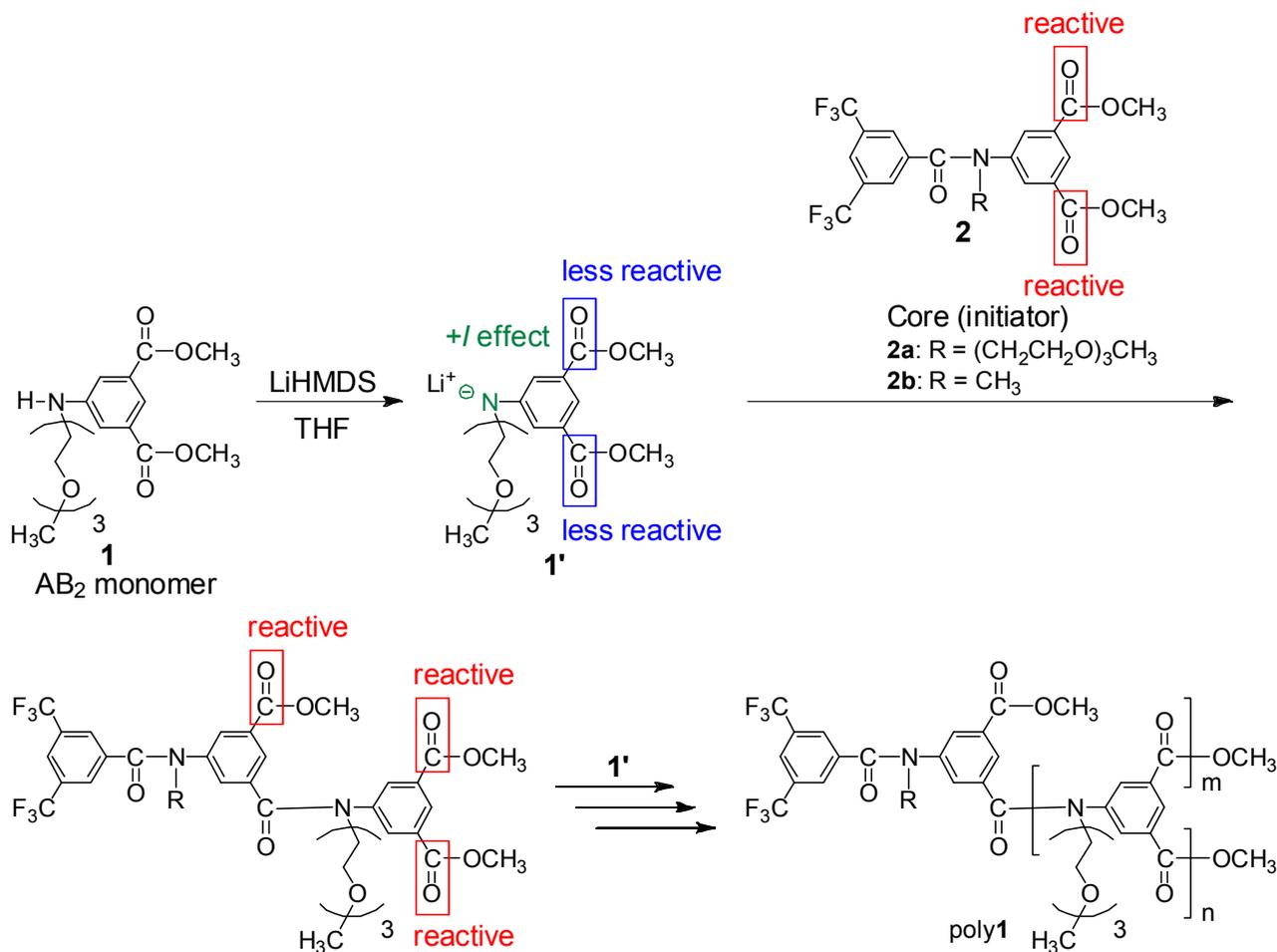
Abstract: Condensation polymerization of 5-aminoisophthalic acid methyl ester **1** bearing a *N*-tri(ethylene glycol) methyl ester (TEG) chain as an AB₂ monomer was conducted and the properties of the resulting hyperbranched polyamides (HBPA) were investigated. When the polymerization of **1** was carried out with *N*-methyl core initiator **2b** at various feed ratios of **1** to **2b** ($[1]_0/[2b]_0$) in the presence of LiHMDS and LiCl at -10 °C, the M_n values of the obtained HBPA increased in proportion to the $[1]_0/[2b]_0$ ratio from 7 to 46 ($M_n = 3810-18600$), retaining a narrow molecular weight distribution ($M_w/M_n = 1.11-1.19$). The HBPA was soluble in water, and a 0.25 wt.-% aqueous solution of the HBPA exhibited a lower critical solution temperature (LCST). The cloud point was 21–23 °C, which is about 30 °C lower than that of the corresponding poly(*m*-benzamide) with the *N*-TEG unit.

Keywords: hyperbranched polymer; chain-growth condensation polymerization; LCST; thermally responsive polymer

1. Introduction

Dendritic macromolecules, such as dendrimers and hyperbranched polymers, have received considerable attention in recent years because of their unusual properties arising from their unique molecular architecture [1–9]. The synthesis of dendrimers is often tedious, whereas hyperbranched polymers can be synthesized by one-step polymerization of AB_m ($m \geq 2$) type monomers. However, hyperbranched polymers obtained by general synthetic methods possess uncontrolled molecular weight and broad molecular weight distributions because of the use of polycondensation or polyaddition reactions that proceed via a step-growth polymerization mechanism. The physical properties of hyperbranched polymers depend on the chemical composition, molecular weight, molecular weight distribution, and degree of branching (DB), and therefore it is desirable to develop a new controlled polymerization method that can afford polymers with defined molecular weight and low polydispersity. Slow addition of monomers to a core molecule [10–14] and the use of highly reactive core molecules [15] have been reported. In both cases, however, the deviation of the observed molecular weight from the calculated value, based on the feed ratio of the monomer to the core ($[\text{monomer}]_0/[\text{core}]_0$), increased and the polydispersity broadened when attempts were made to synthesize higher-molecular-weight polymer. These results probably reflect unsatisfactory suppression of self-polymerization of the monomer. Chain-growth polymerization essentially does not induce self-polymerization, and the ring-opening isomerization polymerization of cyclic latent AB_2 monomers from a core molecule yielded hyperbranched polymers with controlled molecular weight ($M_n = 2000\text{--}3000$) and relatively low polydispersity ($M_w/M_n = 1.3\text{--}1.5$) [16,17]. However, polymers with higher molecular weight were precipitated during polymerization.

Recently, we have reported a novel chain-growth condensation polymerization of 5-(*N*-alkylamino)benzoic acid ester as a AB_2 monomer with a core initiator, yielding hyperbranched polyamide (HBPA) with a narrow molecular weight distribution and controlled molecular weight depending on the feed ratio of the monomer to the core [18,19]. This method utilizes the change of substituent effects between the monomer and the polymer, in which the polymer terminal B group becomes more reactive than the B group of the AB_2 monomer, resulting in suppression of self-polymerization of the monomer. The obtained HBPA showed different solubility, glass transition temperature (T_g), 10% weight-loss temperature (T_d^{10}), and surface segregation in a linear polystyrene matrix when the *N*-alkyl group of HBPA was changed [19,20]. Before this investigation, we had found that poly(*m*-benzamide) with tri(ethylene glycol) methyl ether (TEG) side chains on the amide nitrogens is soluble in water, even though the backbone is aromatic polyamide, and exhibited a lower critical solution temperature (LCST) [21]. This fact led us to wonder whether an AB_2 monomer with the TEG side chain would undergo chain-growth condensation polymerization to yield water-soluble HBPA. In this paper, we describe the chain-growth condensation polymerization of 5-aminoisophthalic acid methyl ester **1** with the TEG unit on the amino group from core initiator **2**, yielding well-defined, water-soluble HBPA (Scheme 1). Taking advantage of the controlled polymerization of **1**, we further investigated the LCST of the obtained HBPA in relation to molecular weight.

Scheme 1. Polymerization of monomer **1** with initiator **2**.

2. Results and Discussion

2.1. Polymerization Conditions

The polymerization of **1** with 3.2 mol% of initiator core **2a** was carried out by the addition of **1** over 50 min to a mixture of 1.1 equiv of lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS) and 5 equiv of *N,N,N',N'*-tetramethylethylenediamine (TMEDA), which is the best additive for the chain-growth condensation polymerization of methyl 3-aminobenzoates bearing the *N*-TEG unit [21], in THF at $-30\text{ }^\circ\text{C}$ (Table 1, Entry 1). The molecular weight distribution of the obtained HBPA, poly**1**, was relatively narrow ($M_w/M_n = 1.33$), but it was broader than that of polymers obtained by the polymerization of methyl 3-aminobenzoates bearing the *N*-TEG unit [21] or of ethyl or methyl 5-(*N*-alkylamino)isophthalates [18,19] ($M_w/M_n < 1.19$). On the other hand, controlled polymerization of 5-(*N*-alkylamino)isophthalic acid ester monomers requires LiCl as an additive to suppress self-polymerization, because LiCl decreases the reactivity of the amide anion generated from the monomer, thereby preventing the reaction of the LiCl-stabilized amide anion with the ester moiety of the non-deprotonated monomer [18,19]. Thus, the polymerization of **1** was next conducted in the presence of 5 equiv of LiCl at $-30\text{ }^\circ\text{C}$ (Entry 2). The polydispersity ($M_w/M_n = 1.32$) became slightly lower than that of the polymer obtained in the presence of TMEDA, but was still higher than that of HBPA with alkyl groups ($M_w/M_n = 1.07\text{--}1.16$). Furthermore, the polymerization proceeded more

slowly than that of ethyl or methyl 5-(*N*-alkylamino)isophthalate, implying that the deprotonation of **1** with LiHMDS was slower than in the case of ethyl or methyl 5-(*N*-alkylamino)isophthalate.

Table 1. Polymerization of **1** with **2a**^(a).

Entry	Additive	[1] ₀ /[2a] ₀	Temp (°C)	Reaction time (h)	<i>M</i> _n ^(b)	<i>M</i> _w / <i>M</i> _n ^(b)
1	TMEDA	31	−30	15	4760	1.33
2	LiCl	35	−30	24	5370	1.32
3	LiCl	31	−20	3	4970	1.32
4	LiCl	30	−10	1	5250	1.29
5	LiCl	33	0	0.17	4850	1.47

^(a) Polymerization of **1** with **2a** was carried out in the presence of 1.1 equiv of LiHMDS and 5 equiv of additive in THF ([**1**]₀ = 0.11 M); ^(b) Determined by GPC based on polystyrene standards (eluent: THF).

Accordingly, the polymerization was carried out at a temperature higher than −30 °C in the presence of LiCl. The polymerization at −20 °C proceeded faster, but the molecular weight distribution was the same as it was at −30 °C (Entry 3). The polymerization at −10 °C afforded poly**1a** with lower polydispersity (Entry 4). However, the increase of the polymerization temperature to 0 °C resulted in a broader molecular weight distribution (Entry 5). Therefore, the optimal polymerization temperature was considered to be −10 °C.

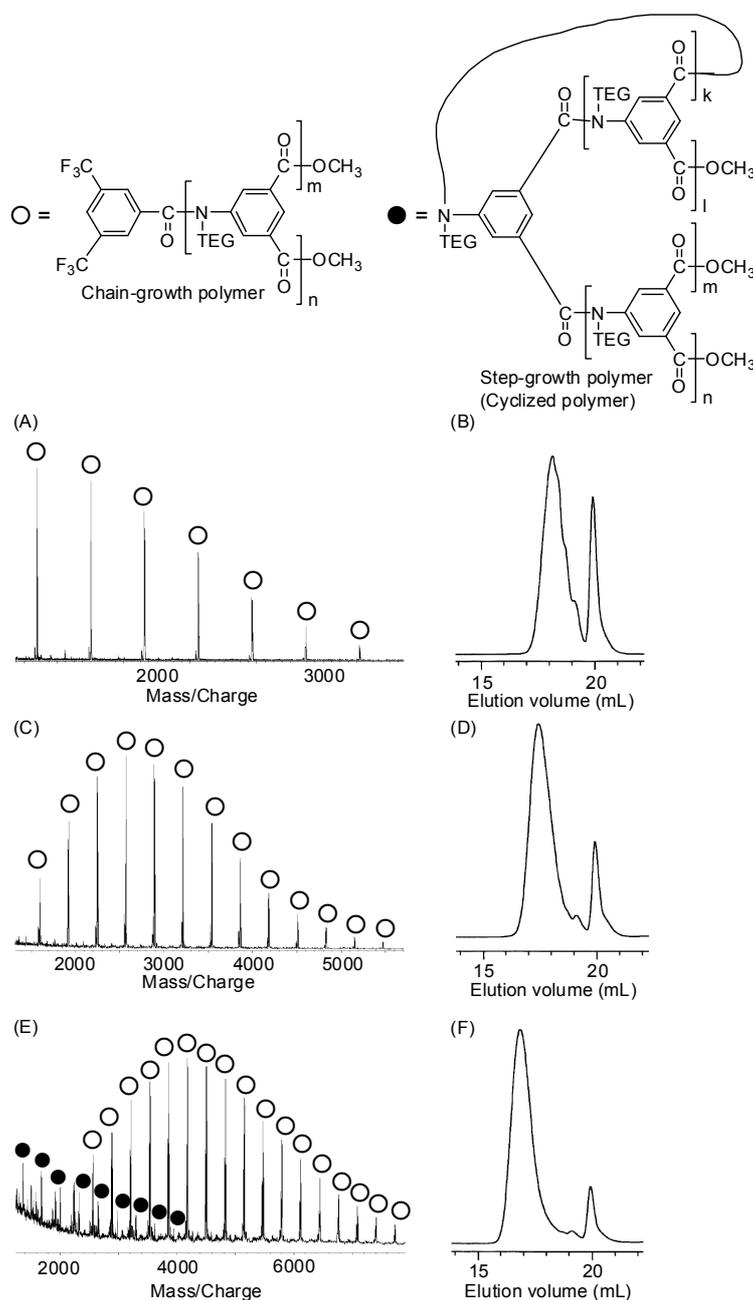
2.2. Effect of *N*-TEG Chain on Polymerization

The polymerization of **1** with **2a** afforded HBPA with somewhat broader molecular weight distribution, contrary to the polymerization of *N*-alkyl monomer with *N*-alkyl initiator. To clarify the effect of the *N*-TEG chain of **1** on the polymerization, we checked the polymer end groups during polymerization by examining aliquots of the reaction mixture withdrawn during addition of **1** to the mixture of LiHMDS and **2a**. The matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra, using dithranol as a matrix in the presence of potassium trifluoroacetate as a cationizing salt, showed only one series of peaks due to HBPA with the **2a** core unit until a quarter of the **1** had been added (Figure 1A,C). Clear peaks corresponding to HBPA without the **2a** unit, in which the amino group has intramolecularly reacted with one of the ester moieties to form a cyclic structure, appeared when a half of the **1** had been added (Figure 1E). Furthermore, the polydispersity of poly**1** became broader with the course of addition of the monomer (1/8 of **1** added: *M*_n = 1620, *M*_w/*M*_n = 1.17; 1/4 of **1**: *M*_n = 2530, *M*_w/*M*_n = 1.21; 1/2 of **1**: *M*_n = 3700, *M*_w/*M*_n = 1.25) (Figure 1B,D,F).

This behavior was exactly the same as that reported in the case of the polymerization of ethyl 5-(methylamino)isophthalate with an initiator in the *absence* of LiCl [19]. Thus, the proton abstraction from the amino group of **1** slowed down as the base concentration decreased from the middle stage, and self-polymerization would be initiated by the reaction of **1**, not the deprotonated compound, with the amide anion generated from **1**. In the polymerization of *N*-alkyl monomer in the *presence* of LiCl, the reaction of the LiCl-stabilized amide anion with the ester moiety of the monomer would be prevented, resulting in chain-growth condensation polymerization to yield HPBA with low polydispersity. Consequently, LiCl would not effectively stabilize the amide anion **1**' in the

polymerization of **1**, probably because the TEG chain of **1** coordinates Li cation, interfering with the stabilization of the amide anion **1'** with Li cation at the anionic site.

Figure 1. MALDI-TOF mass spectra and GPC profiles of HBPA in samples taken during addition of **1** to the reaction mixture of 1.1 equiv of LiHMDS in THF ($[1]_0/[2a]_0 = 31$, $[1]_0 = 0.11$ M) at (A) and (B) 1/8, (C) and (D) 1/4, (E) and (F) 1/2 of **1** added.



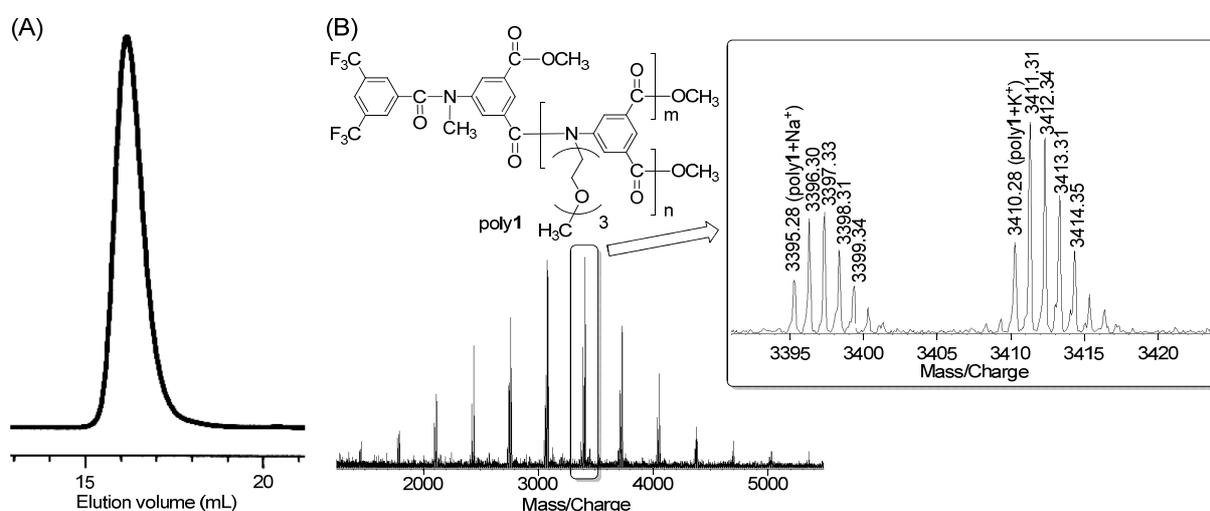
2.3. Effect of Initiator

Although we mentioned in the previous section that the production of HBPA with somewhat broader molecular weight distribution was due to the propensity of **1** to undergo self-polymerization because of coordination of the TEG chain to Li cation, we could not rule out the cause of slow initiation by using **2a**. Indeed, we confirmed slow consumption of **2a** by means of thin layer

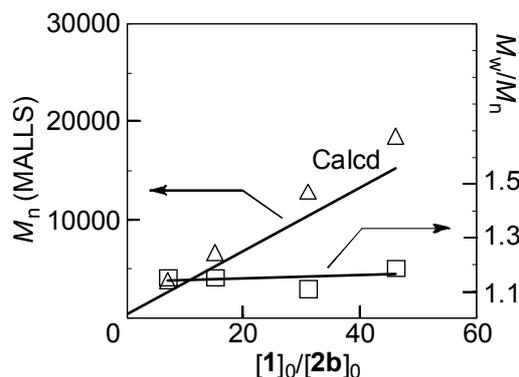
chromatography (TLC) of the polymerization mixture. Accordingly, we tried to polymerize **1** with *N*-methyl initiator **2b**, apparently a smaller *N*-substituent than the TEG unit, in the presence of LiHMDS and LiCl in THF at $-10\text{ }^{\circ}\text{C}$. The GPC chromatogram of the obtained poly**1** surprisingly showed a very narrow, monomodal peak ($M_w/M_n = 1.11$) (Figure 2A). The M_n value of hyperbranched polymer estimated by GPC is generally lower than the real M_n value and therefore the M_w value was determined with a multiangle laser light scattering (MALLS) detector. To facilitate comparison with the theoretical value ($M_n(\text{calcd})$) based on the monomer/core initiator feed ratio, the M_n value designated as $M_n(\text{MALLS})$ was calculated by division of the M_w value from MALLS by the M_w/M_n ratio from GPC. The $M_n(\text{MALLS})$ of the above polymer was 12900, which is close to the theoretical value ($M_n(\text{calcd}) = 10500$).

The polymer end group of the HBPA was analyzed by MALDI-TOF mass spectrometry. The mass spectrum of the HBPA contains two series of peaks due to the K^+ and Na^+ adducts of HBPA with the core **2b** unit. No peaks corresponding to the HBPA without the **2b** unit, formed via self-polymerization of **1**, were observed (Figure 2B).

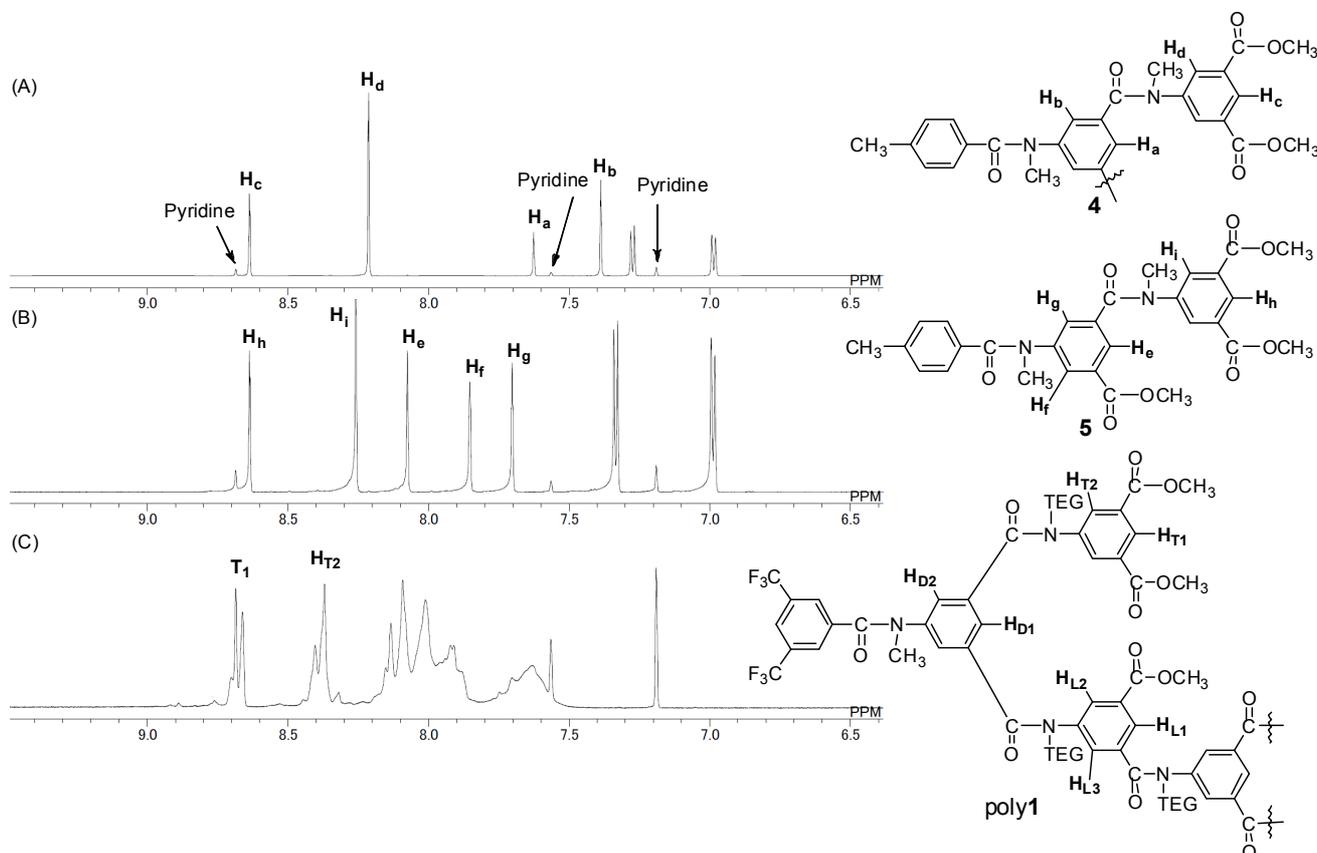
Figure 2. (A) GPC profile of HBPA obtained by the polymerization of **1** with **2b** in the presence of LiHMDS and LiCl in THF at $-10\text{ }^{\circ}\text{C}$ ($[\mathbf{1}]_0/[\mathbf{2b}]_0 = 31$, $[\mathbf{1}]_0 = 0.11\text{ M}$); (B) MALDI-TOF mass spectra of HBPA obtained by the polymerization of **1** with **2b** in the presence of LiHMDS and LiCl in THF at $-10\text{ }^{\circ}\text{C}$ ($[\mathbf{1}]_0/[\mathbf{2b}]_0 = 7$, $[\mathbf{1}]_0 = 0.11\text{ M}$).



Furthermore, the polymerization of **1** with **2b** was carried out with various feed ratios of **1** to **2b** ($[\mathbf{1}]_0/[\mathbf{2b}]_0$), and it turned out that the observed M_n value of poly**1** increased in proportion to the $[\mathbf{1}]_0/[\mathbf{2b}]_0$ ratio from 7 to 46, with the retention of a narrow molecular weight distribution (Figure 3). These results indicate that the polymerization of **1** with **2b** proceeds in a chain-growth polymerization manner.

Figure 3. M_n and M_w/M_n values of poly1 as a function of the feed ratio of 1 to 2b.

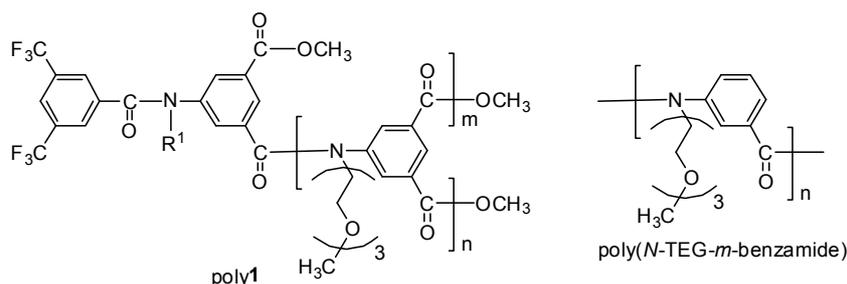
We attempted to estimate the degree of branching (DB) of poly1 by comparison with model compounds of the dendritic and linear units in the same manner as used to estimate the DB of HBPA's with *N*-alkyl groups [18,19]. However, due to the dendritic unit of poly1, the signal of H_{D2} was not observed at the chemical shift as expected from H_b of the dendritic model 4 (Figure 4). The signal of H_{D2} might have shifted to a lower magnetic field in comparison to the corresponding H_{D2} signal of HBPA's with *N*-alkyl groups. Therefore, the DB of poly1 could not be estimated.

Figure 4. 1H NMR spectra in C_5D_5N at 100 °C: (A) 4, (B) 5, (C) HBPA obtained by the polymerization of 1 with 2b in the presence of LiHMDS and LiCl in THF ($[1]_0/[2b]_0 = 31$, $[1]_0 = 0.11$ M).

2.4. Solubility and Aqueous Solution Behavior of Poly1

The solubility of poly1 was examined in various organic solvents and compared with that of linear poly(*m*-benzamide) with the *N*-TEG unit (poly(*N*-TEG-*m*-benzamide)). Poly1 was insoluble in nonpolar solvents such as hexane and ether, but soluble in a wide range of organic solvents (Table 2). Furthermore, poly1 was soluble in not only organic solvents, but also water, although it was less soluble in water than poly(*N*-TEG-*m*-benzamide). These solubility characteristics are similar to those of poly(*N*-TEG-*m*-benzamide) [21].

Table 2. Solubility of poly1 and poly(*N*-TEG-*m*-benzamide)^a.



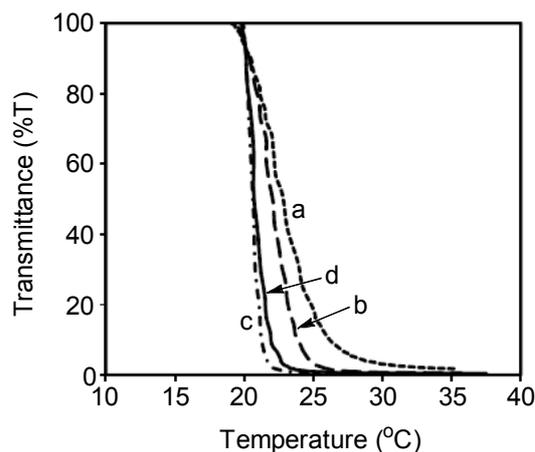
Solvent	poly1	poly(<i>N</i> -TEG- <i>m</i> -benzamide)
Hexane	–	–
Ether	–	–
Toluene	+	+
CH ₂ Cl ₂	+	+
Ethyl acetate	+	+
Acetone	+	+
CH ₃ CN	+	+
DMF	+	+
DMSO	+	+
Ethanol	+	+
Methanol	+	+
H ₂ O	+	+

^a +: soluble; –: insoluble.

The aqueous solution of poly1 exhibited a cloud point when heated in a similar manner to poly(*N*-TEG-*m*-benzamide). Thus, the LCST of 0.25 wt.-% aqueous solutions was measured by monitoring the transmittance of a 500 nm light beam through a 1 cm quartz sample cell with a heating scan at a rate of 0.5 °C/min (Figure 5). Phase separation of poly1 with low molecular weight ($M_n = 3810$, $M_w/M_n = 1.15$) gradually occurred between 19–35 °C (Figure 5, curve a), whereas the solubility of poly1s with higher molecular weight ($M_n = 12900$, $M_w/M_n = 1.11$; $M_n = 18600$, $M_w/M_n = 1.19$) sharply altered between 20–25 °C (curves c and d). This result indicated that the thermotransition of poly1 in an aqueous solution becomes sharper with increasing molecular weight until the molecular weight exceeds a certain value. The cloud point of poly1 was 21–23 °C, which was about 30 °C lower than that of a 0.5 wt.-% aqueous solution of poly(*N*-TEG-*m*-benzamide) [21]. One might think that the cloud point of hyperbranched polymer would be higher than that of the corresponding linear polymer because the former is generally more soluble than the latter. We

speculate that when dissolved in water, poly(*N*-TEG-*m*-benzamide) might adopt a particular conformation, such as folded backbone and extended TEG chain whereas poly1 does not have sufficient flexibility to adopt such a conformation in water, resulting in a lower cloud point.

Figure 5. Transmittance versus temperature curves (500 nm, 0.5 °C/min) obtained for 0.25 wt.-% aqueous solutions of poly1 (curve a: $M_n = 3810$, $M_w/M_n = 1.15$; curve b: $M_n = 6760$, $M_w/M_n = 1.15$; curve c: $M_n = 12900$, $M_w/M_n = 1.11$; curve d: $M_n = 18600$, $M_w/M_n = 1.19$).



3. Experimental Section

3.1. Measurements

^1H , ^{13}C and ^{19}F NMR spectra were obtained on JEOL ECA-600 and ECA-500 instruments operating in the pulsed Fourier-transfer (FT) mode, using tetramethylsilane (TMS, 0.00 ppm) and the midpoint of CDCl_3 (77.0 ppm) as internal standards for ^1H and ^{13}C NMR spectra, and C_6F_6 (0.00 ppm) as an external standard for ^{19}F NMR. IR spectra were recorded on a JASCO FT/IR-410. The M_n and M_w/M_n values of polymers were measured on a Shodex GPC-101 (eluent: THF; calibration, polystyrene standards) equipped with Shodex UV-41, Shodex RI-71S, and Wyatt Technology DAWN EOS multiangle laser light scattering (MALLS, Ga-As laser, $\lambda = 690$ nm) detectors and two Shodex KF-804-L columns. MALDI-TOF mass spectra were recorded on a Shimadzu/Kratos AXIMA-CFR plus in the reflectron ion mode with the use of a laser ($\lambda = 337$ nm). Dithranol (1,8-dihydroxy-9[10H]-anthracenone) was used as the matrix for the MALDI-TOF mass measurements. The solubility of poly1 was examined by 2 mg of the polymer in 1 mL of solvents. The phase transition of poly1 in water was determined by monitoring the transmittance with a Shimadzu UV-2500PC UV/vis spectrometer. The transmittance of 0.25 wt.-% polymer solution at 500 nm was monitored in a cell (path length of 1.0 cm) at a heating rate of 0.5 °C/min.

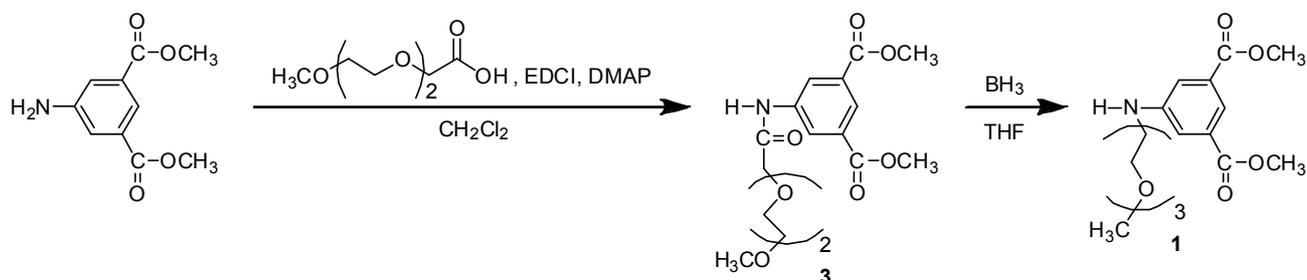
3.2. Materials

Lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, Aldrich; 1.0 M solution in THF), dehydrated tetrahydrofuran (dry THF, Kanto) and dehydrated dichloromethane (dry CH_2Cl_2 , Kanto) were used as

received. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was distilled over CaH_2 . Initiator **2b** and model compounds of dendritic **4** and linear **5** units were prepared according to the literature [18,19].

3.3. Synthesis of Monomer 1

Scheme 2. Synthesis of monomer **1**.

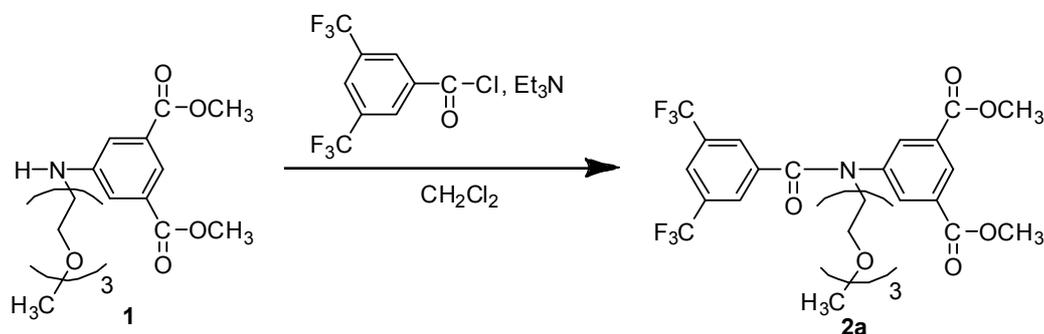


3.3.1. Compound 3

To a solution of 5-aminoisophthalic acid methyl ester (4.99 g, 23.9 mmol) in dry CH_2Cl_2 (75 mL) were added 2-[2-(2-methoxyethoxy)ethoxy]acetic acid (4.5 mL, 29 mmol) and 4-(dimethylamino)pyridine (DMAP) (3.53 g, 28.9 mmol), followed by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (6.00 g, 31.3 mmol), at $0\text{ }^\circ\text{C}$. The mixture was stirred at room temperature for 18 h, then the reaction was quenched with water. The whole mixture was extracted with CH_2Cl_2 , and the combined organic layers were washed with 1 M HCl, sat. NaHCO_3 , and brine, followed by drying over anhydrous MgSO_4 . The solvent was removed in vacuo and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/1) to give 7.90 g of **3** as a colorless solid (87%): mp $96.0\text{--}98.1\text{ }^\circ\text{C}$; $^1\text{H NMR}$ (600 MHz, CDCl_3) 9.11 (br s, 1 H), 8.47 (t, $J = 1.4\text{ Hz}$, 1 H), 8.45 (d, $J = 1.4\text{ Hz}$, 2 H), 4.15 (s, 2 H), 3.95 (s, 6 H), 3.80–3.75 (m, 6 H), 3.63–3.62 (m, 2 H), 3.31 (s, 3 H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) 168.7, 165.9, 138.0, 131.3, 126.4, 125.1, 71.7, 71.3, 70.6, 70.3, 70.1, 58.9, 52.4; IR (KBr) 3312, 2925, 2887, 1736, 1685, 1561, 1439, 1249, 1102, 1001, 859, 757 cm^{-1} .

3.3.2. Monomer 1

A solution of **3** (1.37 g, 3.71 mmol) in dry THF (10 mL) was added to 1.03 M borane-THF complex in THF (5.5 mL, 5.7 mmol) at $0\text{ }^\circ\text{C}$. The mixture was stirred under reflux for 8 h, then cooled to room temperature. 6 M HCl was added to the reaction mixture, followed by heating at reflux for 1 h. After the reaction mixture was cooled to room temperature, sat. NaHCO_3 was added, and the whole mixture was extracted with CH_2Cl_2 . The combined organic layers were washed with water and dried over anhydrous MgSO_4 . The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/1) to give 0.931 g of **1** as a light yellow liquid (70%); $^1\text{H NMR}$ (600 MHz, CDCl_3) 7.99 (t, $J = 1.4\text{ Hz}$, 1 H), 7.46 (d, $J = 1.4\text{ Hz}$, 2 H), 4.53 (br s, 1 H), 3.92 (s, 6 H), 3.73 (t, $J = 5.2\text{ Hz}$, 2 H), 3.67–3.66 (m, 6 H), 3.58–3.56 (m, 2 H), 3.40 (s, 3 H), 3.38–3.35 (m, 2 H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) 166.7, 148.5, 131.3, 119.4, 117.7, 71.9, 70.54, 70.52, 70.3, 69.2, 59.0, 52.1, 43.4; IR (KBr) 3387, 2951, 2877, 1720, 1606, 1439, 1353, 1313, 1244, 1104, $1004, 758\text{ cm}^{-1}$.

3.4. Synthesis of Initiator **2a**Scheme 3. Synthesis of initiator **2a**.

To a solution of **1** (0.251 g, 0.706 mmol) and triethylamine (0.12 mL, 0.84 mmol) in dry CH_2Cl_2 (2.0 mL) at 0 °C was slowly added a solution of 3,5-bis(trifluoromethyl)benzoyl chloride (0.248 g, 0.894 mmol) in dry CH_2Cl_2 (1.0 mL). The resulting solution was stirred at room temperature for 15 h, followed by the addition of a solution of 3,5-bis(trifluoromethyl)benzoyl chloride (0.124 g, 0.447 mmol) in dry CH_2Cl_2 (1.0 mL). The reaction mixture was stirred at room temperature for 1 h, the reaction was quenched with water, and the whole mixture was extracted with CH_2Cl_2 . The combined organic layers were washed with 1 M HCl and sat. NaHCO_3 , and then dried over anhydrous MgSO_4 . The solvent was removed in vacuo, and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate = 1/1) to give 0.384 g of **2a** as a yellow viscous liquid (91%); ^1H NMR (600 MHz, CDCl_3) 8.51 (s, 1 H), 8.02 (s, 2 H), 7.85–7.65 (m, 3 H), 4.17–4.07 (m, 2 H), 3.91 (s, 6 H), 3.85–3.79 (m, 2 H), 3.65–3.63 (m, 4 H), 3.62–3.60 (m, 2 H), 3.52–3.50 (m, 2 H), 3.35 (s, 3 H); ^{13}C NMR (150 MHz, CDCl_3) 167.4, 164.9, 141.9, 137.5, 133.0, 131.9, 131.5 (q, $J = 34.0$ Hz), 129.3, 128.9–128.8 (m), 123.5–123.4 (m), 122.6 (q, $J = 273.1$ Hz), 71.8, 70.5, 70.46, 70.45, 68.0, 58.9, 52.6, 50.8; ^{19}F NMR (470 MHz, CDCl_3) 98.7; IR (KBr) 3082, 2877, 1731, 1660, 1598, 1439, 1401, 1281, 1135, 1002, 906, 760, 706 cm^{-1} .

3.5. Polymerization of Monomer **1** with Initiator **2b** in the Presence of LiCl

LiCl (0.155 g, 3.66 mmol) was placed in a flask equipped with a three-way stopcock, and dried at 250 °C under reduced pressure. The flask was cooled to room temperature under an argon atmosphere, and then charged with 1.0 M LiHMDS in THF (0.72 mL, 0.72 mmol). The flask was cooled to –30 °C under an argon atmosphere with stirring. A solution of **2b** (0.0100 g, 0.0215 mmol) in dry THF (1.0 mL) under dry nitrogen was added to the flask, followed by a solution of **1** (0.235 g, 0.661 mmol) in dry THF (4.0 mL), added dropwise over *ca.* 50 min at –10 °C with stirring under dry nitrogen. The mixture was stirred at –10 °C for 1 h, and then the reaction was quenched with sat. NH_4Cl . The whole mixture was extracted with CH_2Cl_2 . The organic layer was washed with water, dried over anhydrous MgSO_4 , and concentrated under reduced pressure. The residue was purified by preparative HPLC (eluent: CHCl_3) to give 0.164 g of poly**1** as a yellow solid (72%, M_n (MALLS) = 12900, $M_w/M_n = 1.11$).

4. Conclusions

We have demonstrated that the condensation polymerization of 5-aminoisophthalic acid methyl ester **1** bearing the TEG unit on the amino group with *N*-methyl initiator **2b** proceeds via a chain-growth condensation polymerization mechanism to yield well-defined hyperbranched polyamide (HBPA) with *N*-TEG chains (poly**1**). The initiator was crucial to obtain poly**1** with low polydispersity: the polydispersity was about 1.3 when *N*-TEG initiator **2a** was used, whereas it was about 1.1 when *N*-methyl initiator **2b** was used. The obtained poly**1** was soluble in not only a variety of organic solvents, but also water. Furthermore, 0.25 wt.-% aqueous solution of poly**1** showed a lower critical solution temperature (LCST), and the cloud point was 21–23 °C, which is about 30 °C lower than that of poly(*N*-TEG-*m*-benzamide). Further studies on the synthesis and properties of novel architectures containing well-defined HBPA with the *N*-TEG unit are in progress.

Acknowledgments

This work was supported in part by a Grant-in-Aid (19550128) for Scientific Research from the Japan Society for the Promotion of Science (JSPS) and a Scientific Frontier Research Project grant from the Ministry of Education, Culture, Sports, Science and Technology, Japan. We thank *Masayoshi Watanabe* and *Yuzo Kitazawa*, *Yokohama National University*, for their help in UV/vis spectroscopy to monitor phase separations of aqueous polymer solutions.

References

1. Zeng, F.; Zimmerman, S.C. Dendrimers in supramolecular chemistry: From molecular recognition to self-assembly. *Chem. Rev.* **1997**, *97*, 1681–1712.
2. Bosman, A.W.; Janssen, H.M.; Meijer, E.W. About dendrimers: Structure, physical properties, and applications. *Chem. Rev.* **1999**, *99*, 1665–1688.
3. Grayson, S.M.; Fréchet, J.M.J. Convergent dendrons and dendrimers: From synthesis to applications. *Chem. Rev.* **2001**, *101*, 3819–3868.
4. Tomalia, D.A.; Fréchet, J.M.J. Discovery of dendrimers and dendritic polymers: A brief historical perspective. *J. Polym. Sci. Part A Polym. Chem.* **2002**, *40*, 2719–2728.
5. Fréchet, J.M.J. Dendrimers and other dendritic macromolecules: From building blocks to functional assemblies in nanoscience and nanotechnology. *J. Polym. Sci. Part A Polym. Chem.* **2003**, *41*, 3713–3725.
6. Kim, Y.H. Hyperbranched polymers 10 years after. *J. Polym. Sci. Part A Polym. Chem.* **1998**, *36*, 1685–1698.
7. Gao, C.; Yan, D. Hyperbranched polymers: From synthesis to applications. *Prog. Polym. Sci.* **2004**, *29*, 183–275.
8. Voit, B. Hyperbranched polymers—all problems solved after 15 years of research? *J. Polym. Sci. Part A Polym. Chem.* **2005**, *43*, 2679–2699.
9. Voit, B.I.; Lederer, A. Hyperbranched and highly branched polymer architectures—Synthetic strategies and major characterization aspects. *Chem. Rev.* **2009**, *109*, 5924–5973.

10. Sunder, A.; Hanselmann, R.; Frey, H.; Mulhaupt, R. Controlled synthesis of hyperbranched polyglycerols by ring-opening multibranching polymerization. *Macromolecules* **1999**, *32*, 4240–4246.
11. Bharathi, P.; Moore, J.S. Controlled synthesis of hyperbranched polymers by slow monomer addition to a core. *Macromolecules* **2000**, *33*, 3212–3218.
12. Möck, A.; Burgath, A.; Hanselmann, R.; Frey, H. Synthesis of hyperbranched aromatic homo- and copolyesters via the slow monomer addition method. *Macromolecules* **2001**, *34*, 7692–7698.
13. Kainthan, R.K.; Muliawan, E.B.; Hatzikiriakos, S.G.; Brooks, D.E. Synthesis, characterization, and viscoelastic properties of high molecular weight hyperbranched polyglycerols. *Macromolecules* **2006**, *39*, 7708–7717.
14. Bharathi, P.; Moore, J.S. Solid-supported hyperbranched polymerization: Evidence for self-limited growth. *J. Am. Chem. Soc.* **1997**, *119*, 3391–3392.
15. Bernal, D.P.; Bedrossian, L.; Collins, K.; Fossum, E. Effect of core reactivity on the molecular weight, polydispersity, and degree of branching of hyperbranched poly(arylene ether phosphine oxide)s. *Macromolecules* **2003**, *36*, 333–338.
16. Suzuki, M.; Ii, A.; Saegusa, T. Multibranching polymerization: Palladium-catalyzed ring-opening polymerization of cyclic carbamate to produce hyperbranched dendritic polyamine. *Macromolecules* **1992**, *25*, 7071–7072.
17. Suzuki, M.; Yoshida, S.; Shiraga, K.; Saegusa, T. New ring-opening polymerization via a π -allylpalladium complex. 5. multibranching polymerization of cyclic carbamate to produce hyperbranched dendritic polyamine. *Macromolecules* **1998**, *31*, 1716–1719.
18. Ohta, Y.; Fujii, S.; Yokoyama, A.; Furuyama, T.; Uchiyama, M.; Yokozawa, T. Synthesis of well-defined hyperbranched polyamides by condensation polymerization of ab_2 monomer through changed substituent effects. *Angew. Chem. Int. Ed.* **2009**, *48*, 5942–5945.
19. Ohta, Y.; Kamijyo, Y.; Fujii, S.; Yokoyama, A.; Yokozawa, T. Synthesis and properties of a variety of well-defined hyperbranched n -alkyl and n -h polyamides by chain-growth condensation polymerization of ab_2 monomers. *Macromolecules* **2011**, *44*, 5112–5122.
20. Hirai, T.; Huan, L.; Ohta, Y.; Yokozawa, T.; Tanaka, K. Surface segregation of well-defined n -substituted hyperbranched polyamides in linear polymer matrix. *Chem. Lett.*, **2011**, *40*, 366–367.
21. Sugi, R.; Ohishi, T.; Yokoyama, A.; Yokozawa, T. Novel water-soluble poly(m -benzamide)s: Precision synthesis and thermosensitivity in aqueous solution. *Macromol. Rapid Commun.* **2006**, *27*, 716–721.