Chem 466
Lecture #12
02/25/2014

- Kris Matyjaszewski's Frontier lectures
today @ 5 pm 3 2104
tomorrow @ 4 pm 3

- Exam II, March 6, next Thursday.

March 5 office hours...
old exam II examples to be posted on website today

- Quiz #5: $X = 4.4$ (range 0-14)
  S.D. = 3.6

4 bonus pts for 4-step drug conjugation strategy
• Unique viscosities for dendrimers
  - Generations of growth involve addition of layers of monomers

G = gen #

\[ r_0 = \text{repeat unit length} \]

\[ M_0 = \text{repeat unit mol. wt.} \]

\[ \Rightarrow \text{volume increases cubically, because hydrodynamic radius, } r_h, \text{ increases linearly (ideally)} \]

\[ r_h \propto G \cdot r_0 \]

\[ V_h \propto \frac{4}{3} \pi r_h^3 \]

\[ V_h \propto G \cdot V_h \]

\[ (r_0)^3 \]

\[ V_h \propto G \cdot V_h \]

\[ \Rightarrow \text{mass increases exponentially} \]

\[ \text{e.g., for } A_2B \text{ monomer system grown from a core} \]

\[ \text{mol. mass } \propto (2^{G-1})M_0 \]

\[ \Rightarrow [N] \text{ goes through a maximum (vol.)} \]

\[ \Rightarrow [N] \text{ goes through a maximum (mass)} \]
Exact Linear Analogs of Dendritic Polyether Macromolecules: Design, Synthesis, and Unique Properties

Craig J. Hawker,*†† Eva E. Malmström,* Curtis W. Frank,* and J. Patrick Kampf

Center for Polymeric Interfaces and Macromolecular Assemblies, IBM Almaden Research Center, 650 Harry Road, San Jose, California 95120-6099
Department of Chemical Engineering, Stanford University, Stanford, California 94305

Received June 19, 1997

The study of dendritic macromolecules has progressed at such a rapid pace in recent years that these novel materials are becoming major areas of interest from both an industrial and academic standpoint.1 Much of this research is based on the assumption that dendrimers are inherently different from linear macromolecules and it is this inherent difference that leads to many of the observed changes in physical properties.2 Unfortunately, this comparison is not valid since the dendritic macromolecules are compared with polydisperse linear polymers of significantly different structure. For example, the unique melt viscosity behavior of dendritic polyethers was compared with linear polystyrene and not with monodisperse linear analogs containing the same number of polymer repeat units based on 3,5-dihydroxybenzyl alcohol.3 In this report, we describe a novel synthetic approach to monodisperse linear analogs of dendritic macromolecules and the use of this strategy for the preparation of the exact linear derivatives of the well-studied polyether dendrimers.4

In designing the synthesis of the linear analogs it became immediately apparent that a traditional exponential growth strategy5 involving the synthesis of dimers, tetramers, octamers, etc. would not be applicable since the number of internal repeat units of the dendrimers increased in a different numerical sequence. For example, both the exact linear analog of the fourth-generation polyether dendrimer 2 and the actual dendrimer 1 must have 15 (2° - 1) internal repeat units which is not consistent with an exponential (2n) approach (Figure 1). A strategy for the accelerated synthesis of linear polymers with 1, 3, 7, 15, 31, (2n − 1) repeat units was therefore developed. The basic strategy, outlined in Schemes 1 and 2 involves a converging dual exponential growth strategy in which two series of linear macromolecules, one with 2n repeat units and the other with 2n−1 repeat units, are prepared and then coupled to give the desired linear analogs. To obtain the exact linear analogs, the deprotected monomeric derivatives (i.e., 9 or 14) are coupled at each generation step with the linear oligomer containing 2n−1 repeat units and a single benzyl ether chain end (i.e., 11 or 13). For example, reaction of the first-generation bromide 11 with the monophenol 9 leads to the exact linear analog 12 of the second-generation dendritic alcohol. Bromination of 12 gives the linear [G-2]-Br derivative 13 which can then be coupled with the next generation linear monophenolic derivative 14 to give the exact linear analog of the third generation alcohol 15 which contains seven repeat units, eight benzyl ether groups, and a single hydroxymethyl chain end.

Repetition of this strategy leads to higher generation linear analogs of the dendritic polyether macromolecules which have exactly the same number of repeat units and pseudo-chain ends as their dendritic equivalents. In essence they are macromolecular isomers of dendrimers and the synthesis has been continued up to the sixth-generation derivative. Using standard techniques developed for dendritic macromolecules, the structure of the exact linear analogs and associated precursor molecules could be confirmed using a combination of 1H and 13C NMR spectroscopy, GPC, and MALDI mass spectrometry. As expected GPC analysis of the linear analogs showed a single peak (polydispersity less than 1.01) while MALDI mass spectrometry showed a single molecular ion corresponding to the expected molecular weight on the basis of the synthetic strategy.

The ability to prepare the exact linear analogs of the polyether dendrimers permits an unprecedented opportunity to study the actual difference between linear and dendritic macromolecules. Initially the three-dimensional molecular size of the linear and dendritic polymers were compared by gel permeation chromatography. Interestingly, a discontinuous relationship between the hydrodynamic volumes of the exact linear analogs and the corresponding dendrimers was observed. For generations four and below, the hydrodynamic volumes of the linear and dendritic macromolecules were essentially the same. However, a marked increase in the hydrodynamic volume for the linear derivatives, compared to the dendritic equivalents, was observed on going to generation five and six. For example, both the fifth generation dendrimer [G-5]-OH, 16, and the exact linear analog 17 with 31 repeat units have molecular formulas of C44H89O30 and nominal molecular weights of 6680. While these materials show the same molecular ion by MALDI, the GPC traces show

Figure 2. GPC traces for the (a) fifth generation dendritic alcohol 16, [G-5]-OH, and (b) the corresponding exact linear analog 17.

a significant difference in retention volume with the linear analog 17, having an approximately 40% larger hydrodynamic volume (Figure 2). This result is fully consistent with the more compact globular structure of the dendrimer in comparison to the random coil structure of its linear analog. It is of particular interest that similar property changes, or discontinuities, between generation four and fifth has been observed for a number of other dendrimer systems and suggests a fundamental difference between linear and dendritic macromolecules may only manifest itself in higher generation materials.

Significant differences were also found when the solubility and crystallinity of the linear and dendritic polyethers were compared. The fifth generation dendrimer 16 is completely amorphous and shows a glass transition temperature of 42 °C. In direct contrast, the exact linear analog 17 is highly crystalline and displays a strong melting transition at 150 °C. This high level of crystallinity was also observed for all other linear analogs and results in significantly different solubility behavior when compared to the amorphous dendrimers. In fact, the linear analogs can be crystallized from THF, acetone, or chloroform; solvents in which the dendrimers are extremely soluble.

In conclusion, a double-exponential growth strategy has been developed and successfully applied to the preparation of the linear analogs of the well-studied polyether dendrimers and the physical properties of the two series of macromolecular isomers compared. Significantly, it is observed that there is essentially no difference in hydrodynamic volume between the linear and dendritic polyethers up to generation four; however, a marked difference occurs for generation five and six with the linear macromolecule having a significantly larger hydrodynamic volume in tetrahydrofuran. It is also observed that the linear analogs are highly crystalline and have low solubilities which is in direct contrast to the amorphous and highly soluble dendrimers.

Acknowledgment. The authors express their gratitude to the NSF Center for Polymeric Interfaces and Macromolecular Assemblies.

Supporting Information Available: Experimental data for compounds discussed in this work (10 pages). See any current masthead page for ordering and Internet access instructions.

JA972027X

organic compounds are synthesized, or divergent, that is the construction of dendrimers can be regarded as a step polymerization with polydispersities of almost 1. Detailed studies show that only a limited number of reaction schemes can be used for the synthesis of these dendrimers; all known methods to date do not deliver pure dendrimers in large quantities, which is due to the use of sophisticated building blocks and/or (large excesses of) expensive reagents and/or complicated purifications. In this paper we present a very convenient reaction sequence for the large-scale production of pure poly(propylene imine) dendrimers.

The reaction sequence presented here (Scheme 1) is based on the first approaches to dendrimeric structures by Vögtle et al. in which the low yields in the reduction hampered the synthesis of higher generations. Our sequence is a repetition of a double Michael addition of acrylonitrile to primary amine groups, followed by the heterogeneously catalyzed hydrogenation of the nitriles, resulting in a doubling of the number of primary amines. In this sequence, 1,4-diaminobutane has been used as the dendrimer core; but a variety of molecules with primary or secondary amine groups can also be used. We have optimized conditions for both reaction steps in the sequence so that this occurs almost quantitatively and with optimal selectivity.

All Michael reactions were performed similarly; 2.5 equivalents of acrylonitrile per primary amine are used at a concentration of 0.1 M in water; the first equivalent of acrylonitrile is added at room temperature and the second equivalent at 80 °C. The reaction time for complete conversion increases with every generation: 1 h for generation 0.5 (DAB-dendr(CN)$_4$), 3 h for generation 4.5 (DAB-dendr(CN)$_{16}$). The excess of acrylonitrile is distilled off as a water azeotrope, leaving a clear two-phase system, from which the pure dendrimers with nitrile end groups can be isolated by pouring off the water layer. If necessary the water-soluble side products for example HOCH$_2$CH$_2$CN (the Michael addition adduct of H$_2$O to acrylonitrile) or incompletely cyanoethylated products can be separated by washing the residue with water.

The hydrogenations of the cyanoethylated structures with H$_2$ and Raney/Cobalt as catalyst are also performed preferably in water. The reaction time required for complete hydrogenation increases at higher generations, but even at the higher generations this heterogeneous hydrogenation is quantitative and selective. Dendrimers with NH$_2$ end groups are isolated by evaporating the water from the filtered reaction mixture. The process window for a quantitative hydrogenation is small and side reactions easily occur. Three major side reactions which lead to dendrimers with structural defects have been observed, and the corresponding side products have been characterized: a) the occurrence of the retro-Michael addition during the hydrogenation, yielding secondary amines, b) incomplete cyanoethylation in the Michael addition, resulting in dendrimers missing one ethyl cyanide side chain, and c) the formation of cyclic di- and NH$_2$H$_2$ by intramolecular addition of amines to the intermediate imines during the hydrogenation reactions. Under the optimized conditions these side products are not detectable and poly(propylene imine) dendrimers can be synthesized up to generation 4.5 with 64 terminal nitrile groups, a molecular weight of 6912 g mol$^{-1}$ and in quantities of several grams up to several kilograms. Apart from the first generation (0.5) which is a white crystalline solid, all other generations are colourless oils, which are readily soluble: the DAB-dendr(NH$_2$)$_{16}$, in H$_2$O and methanol, the DAB-dendr(CN)$_{16}$, in common organic solvents.

All products were characterized by $^1$H, $^{13}$C NMR and IR spectroscopy, mass spectrometry, HPLC, gel permeation chromatography (GPC), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and intrinsic viscosity. All data are consistent with the proposed dendrimer structures. NMR spectroscopy appears to be a very suitable technique to detect and assign structural failures in the outermost dendrimer generation. In the $^1$H NMR spectra of the dendrimers with CN end groups the shape and intensity of the downfield triplet of the NCH$_2$CH$_2$CN group at $\delta$ = 2.85 is characteristic for defects in the outer generation, whilst the growth of the dendrimers is clearly indicated by the ratio of the integrals of the signal at $\delta$ = 1.40 (NCH$_2$CH$_2$CH$_2$N protons of the dendrimer core) to the integral of the signal at $\delta$ = 1.58 (NCH$_2$CH$_2$N branch protons). Incompletely cyanoethylated dendrimers are most readily concluded from additional signals in the $^{13}$C NMR spectra at $\delta$ = 45.1 (NHCH$_2$CH$_2$CN) and 18.7 (NHCH$_2$CH$_2$CN) as well as the products of retro-Michael additions of dendrimers with NH$_2$ end groups with signals at $\delta$ = 47.7, 46.7, 39.1, 32.0, and 25.6.

Dendrimers with CN end groups can be separated and analyzed with HPLC. In Figure 1 a typical chromatogram of DAB-dendr(CN)$_{16}$ from a kg-scale run is shown. From mass spectrometric experiments it has been concluded that the small peak corresponds with the fully cyanoethylated product of DAB-dendr(NH$_2$)$_{16}$. If equal absorption coefficients are assumed for both compounds, the average selectivity per conversion in the first three steps is 99.8%.

Figure 2 shows a typical gel permeation chromatogram of various dendrimers with NH$_2$ end groups taken from a large-scale synthesis. The absence of detectable impurities is evi-
Thermal analysis of the dendrimers synthesized shows a number of interesting features. The glass transition temperature \(T_g\) has been recorded with DSC (Fig. 4); in both series of dendrimers with \(\text{NH}_2\) and \(\text{CN}\) end groups the \(T_g\)'s observed are low and an increase in \(T_g\) is observed by increasing molecular weight as determined by TGA (For DAB-dendr-(\(\text{NH}_2\))\(_4\), DAB-dendr-(\(\text{NH}_2\))\(_6\), DAB-dendr-(\(\text{NH}_2\))\(_8\), DAB-dendr-(\(\text{NH}_2\))\(_{12}\), TGA\(_{\text{max}}\) are 330, 378, 424, and 470°C, respectively. For the DAB-dendr-(\(\text{NH}_2\))\(_6\) less than 1.0% weight loss is observed at \(T = 310^\circ\text{C}\) and scan speed 20°C min\(^{-1}\). Dendrimers with \(\text{CN}\) end groups are less stable, although also in this case the stability increases at higher generations. With TGA-MS, a thermally induced retro-Michael addition is observed for DAB-dendr-(\(\text{CN}\))\(_{14}\), followed by a degradation similar to DAB-dendr-(\(\text{NH}_2\))\(_{12}\). A molecular interpretation of the latter is not possible with the data available.

As a consequence of the extensive purifications and low yields in the first approaches\(^8\) it was assumed until recently that this acrylonitrile-hydrogenation sequence is not suitable for dendrimer synthesis. However, by the correct choice of reagents and reaction conditions we have shown that this reaction sequence is very efficient. The main advantages of our synthetic procedures are 1) the simple reaction and isolation procedures which can readily be scaled up; 2) the use of one solvent for all reaction steps, so that the intermediates must not be isolated; 3) the use of readily available reagents which do not have to be protected; 4) the high yields and selectivities obtained; 5) a simple purification method which can easily be applied to large-scale quantities; 6) the versatility of the reaction sequence which allows for the introduction of a variety of end and core groups.

The dendrimers with \(\text{NH}_2\) end groups offer remarkable thermal and good hydrolytic stability, and have a low \(T_g\). The drop in intrinsic viscosity after the fourth generation indicates that a spherical shape with a sterically hindered shell is formed at the fifth generation. The low \(T_g\) indicates that the dendrimers possess a large degree of conformational freedom, despite their hyperbranching and well-defined chemical and geometrical structure. Research into the synthesis of higher generations and the functionalization of the dendrimers is in progress.

**Experimental Procedure**

DAB-dendr-(\(\text{CN}\))\(_{14}\); Acrylonitrile (8.35 mol, 443 g) was added to a solution of diaminobutane (1.67 mol, 147 g) in 1.176 kg water. The exothermic reaction caused the temperature to rise to 38°C. After this exothermic effect the reaction mixture was heated at 80°C for 1 h to complete the addition. Then the excess of acrylonitrile was removed as a water azeotrope by vacuum distillation (16 mbar, bottom temperature 40°C). Phase separation of the reaction mixture afforded 499 g (99%) HPLC-pure DAB-dendr-(\(\text{CN}\))\(_{14}\), which was recrystallized from methanol.

\(^1^C\) NMR (50 MHz, \(\text{CDCl}_3\)): \(\delta = 119\) (CN), 53.1 (N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)), 49.4 (N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)), 24.9 (N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)), 16.9 (CH\(_2\text{CN}\)). \(^1^H\) NMR (200 MHz, \(\text{CDCl}_3\)): \(\delta = 2.85\) (t, 8H, N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)), 2.55 (m, 4H, N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)), 2.48 (l, 8H, CH\(_2\text{CN}\)). 1.55 (m, 4H, N\(_\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{N}\)); IR (KBr): \(\nu = 2245\) cm\(^{-1}\) (CN).
MALDI-tOF mass spectrometry
(matrix assisted laser desorption ionization - time-of-flight)

- gives mol. wt. distribution w/ higher resolution than SEC, but difficult to quantify d's of each molecular mass species, due to complicated features of desorption, ionization + flight

- does not fragment the polys, allows for mass detm. of 90's kDa

- e.g. Glucose-based Polycarbonates
  GPC vs MALDI-tOF ($M_n$ vs $M_n$ end groups)
  (NMR can also give $M_n$ + end groups)
Glucose-based Polycarbonates: GPC analysis of stoichiometry-promoted molecular weight control

\[ \text{H}_3\text{C} \stackrel{\text{OH}}{\longrightarrow} \text{H}_3\text{CO}-\bigg[\text{C} \sim \text{O} \bigg] \stackrel{\text{H}_3\text{CO}}{\longrightarrow} \text{OCH}_3 \text{H}_3\text{C} \]

\[ [\text{M}]_0/[\text{I}]_0 = 51, 27, 15 \]

Glucose-based Polycarbonates: MALDI-tof analysis of molecular weight and chain ends

MALDI-TOF MS

repeating unit = 248.2298

For example, the 21-mer of this distribution is expected to give a signal at m/z 248.2 × 21 (repeat units) + 121.2 (initiating group) + 1.0 (H, terminating group) + 39.0 (K⁺) = 5373.4 g/mol, and indeed, a signal is observed at 5373.8 g/mol.
Polymer Factory introduces a new product line comprising of linear-dendritic hybrid materials with Polyethylene glycol cores and polyester based dendritic end-groups. The unique selling proposition of these PEG-cored dendrimers highlights the large number of terminal hydroxyl groups available for further functionalization.

Core: PEG 6k or PEG 20k

- Traditional PEG-OH
  - Number of -OH: 2
- PFD-G1-PEG-OH
  - Number of -OH: 4
- PFD-G2-PEG-OH
  - Number of -OH: 8
- PFD-G3-PEG-OH
  - Number of -OH: 16

Potential Applications
- Hydrogels for controlled drug release
- Multifunctional scaffolds
- Tissue engineering
- Drug delivery

Featured Material Properties
- Biocompatible, non-toxic, and water soluble
- Well-defined linear-dendritic hybrid materials
- Low polydispersity (PDI < 1.15)
- Increasing number of functional hydroxyl groups
- Readily functionalized for further modifications

Availability & Price
- Available from 250 mg up to 5 g
- Sold individually or in combinations

PRICE: 1 g PFD-G1-PEG6k-OH ➞ 275 €
3 x 250 mg kit (G1-G3) ➞ 275 €

Inquiry for pricing
Polymer Factory Sweden AB
E-mail: info@polymerfactory.com
Phone: + 46 8 718 42 00
Fax: + 46 8 790 82 83
www.polymerfactory.com
IV. Chain-growth Polycondensations

- Preparation of condensation-type polymers by chain-growth polymer mechanism & kinetics
  - Initiator required
  - Monomer undergoes reaction with initiator & propagating chain end, but not with other monomers
  - Gives control over $D_n$, $M_n$ & can lead to narrow $M_w/M_n$

- Requires clever chemistry

1. Initial development of 1st really well-defined system reported in

- Activated monomer undergoes rxn "only" (ideally) w/ initiator + chain end
- Reactivity (electrophilicity) of initiator > chain end

⇒ approx all chains initiate at same time + propagate @ same rate
A chain end carries initiator unit
A chain end remains reactive

Hypothesis that the polymer should have living character

To probe livingness, measure:
1. mol. wt. distribution
2. Whether \( n = \frac{M_n}{M_w} \)
3. Chain length vs. time \( \% \) conversion
4. Ability to perform chain extension by SEC analysis —

Fig 1

\[ \frac{M_n}{M_w} < 1.1 \text{ over entire range} \]

in agreement with calculated values

Fig 2A

linear inc. in DPn + Mn

\% conversion

Fig 2B

poly after additional monomer added

initial poly (\( 98\% \) conv.)

det. response

retan. vol. →
The polymerization of $I_a$ was carried out in the presence of 1.0 equiv of CsF, 2.0 equiv of 18-crown-6, and phenyl 4-nitrobenzoate 2 as an initiator in THF at room temperature to yield a polyamide quantitatively, which was soluble in THF, chloroform, dichloromethane, N,N-dimethylformamide (DMF), and even toluene. In the polymerization with varying the feed ratio ($|I_a|/|2|$), the MWD of polymers was narrow ($M_n/M_w = 1.16-1.20$) when the $|I_a|/|2|$ ratios were 10 or less but gradually increased up to 1.47 after that. Broad MWD in high $|I_a|/|2|$ ratios may be interpreted in terms of the hydrolysis of the silyl group of monomer $I_a$ with a very small amount of water coming from CsF and/or 18-crown-6. Hydrolyzed $I_b$ would not react as a monomer but eventually worked as an initiator, and the amount of $I_b$ could not be neglected in high $|I_a|/|2|$ ratios. Accordingly, we carried out the polymerization of $I_b$ by using N-triethylsilyl-N-octylaniline 6 as a base generated by CsF. Thus, the aminyll group generated from 6 would abstract the proton of the amino group and by so-called “monomer-addition” experiments where a fresh feed of $I_b$ and 6 was added to the prepolymer ($M_n = 4500$, $M_w/M_n = 1.09$) in the reaction mixture. The added $I_b$ feed was smoothly polymerized. The GPC chromatogram of the product (Figure 2B (b)) clearly shifted toward the higher molecular weight region, while retaining the narrow distribution ($M_n = 10 000$, $M_w/M_n = 1.12$).

This experiment implies that this polycondensation will enable us to synthesize block copolyamides having different aminoalkyl side chains and well-defined sequences. Furthermore, we anticipate that this polycondensation will provide new approaches for the design of nanoarchitectures, which have been achieved by stepwise synthesis of dendritic macromolecules and by living polymerizations of vinyl and cyclic monomers. To elucidate whether chain-growth polymerization takes place in this polycondensation, the polymerization of $I_b$ was carried out in the presence of 5 mol % of 2, and the $M_n$ values and the $M_w/M_n$ ratios were plotted against monomer conversion (Figure 2A). The $M_n$ values increased in proportion to conversion, and the $M_w/M_n$ ratios were less than 1.12 over the whole conversion range. This polymerization behavior agrees with the features of living polymerizations.

Figure 1. $M_n$ and $M_w/M_n$ values of poly$I_b$, obtained with 6 and CsF/18-crown-6 in the presence 2 in THF at 25 °C, as a function of the feed ratio of $I_b$ to 2.

Figure 2. Demonstration of chain-growth polycondensation. (A) $M_n$ and $M_w/M_n$ values of poly$I_b$, obtained with 6 and CsF/18-crown-6 in the presence 2 in THF at 25 °C, as a function of monomer conversion. (B) GPC profile of the monomer addition experiment in THF at room temperature: (a) prepolymer ($|I_b|/|2|$ = 20), conversion = 96%; $M_n = 4500$; (b) postpolymer (added $I_b$/|2| = 24), conversion = 187%; $M_n = 10 000$.

Acknowledgment. This work was supported in part by a Grant-in-Aid (10650873) for Scientific Research from the Ministry of Education, Science, and Culture, Japan.

Supporting Information Available: Synthesis of monomer $I_b$ and polymerization procedure (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA001871B

(13) The $M_n$s of polyamides were estimated by gel permeation chromatography (GPC) based on polystyrene standards. However, the $M_n$s determined by GPC were in good agreement with those determined by $^1$H NMR spectra.


(15) In the monomer-addition experiment, it was crucial to use 0.95 equiv of 6 in the first-stage polymerization. An excess amount of 6 did not react with the polymer end group during polymerization but did after the consumption of monomer to give the amide end group, which could not initiate the polymerization in the second-stage.


(17) For examples, see references in ref 12.
Well-Defined Star-Shaped Poly(p-benzamide) via Chain-Growth Condensation Polymerization: Use of Tetra-Functional Porphyrin Initiator to Optimize Star Polymer Formation

KAZUO YOSHINO, AKIHIRO YOKOVAMA, TSUTOMU YOKOZAWA

Department of Material and Life Chemistry, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221-8686, Japan

Received 20 May 2009; accepted August 2009

Keywords: chain-growth condensation polymerization; living polymerization; polyamides; star polymers; porphyrin

INTRODUCTION

Most star polymers with controlled molecular weight and low polydispersity are synthesized by living polymerization, in which only initiation and propagation reactions, but not chain transfer reaction, take place.1 Accordingly, the obtained star polymers are generally not contaminated with linear polymers. Recently, we have developed chain-growth condensation polymerization,2 a kind of living polymerization yielding condensation polymers with controlled molecular weight and narrow molecular weight distribution. However, synthesis of star-shaped poly(p-benzamide) through this method, using multifunctional initiators, afforded not only the desired star-shaped poly(p-benzamide) via chain-growth polymerization, but also a linear poly(p-benzamide) via self-polycondensation of the monomer when the amount of the initiator was decreased. This contamination with linear polymer was more liable to occur as compared to the case of chain-growth condensation polymerization with a nonfunctional initiator under the same conditions.3 In addition, separation of the products by means of high-performance liquid chromatography (HPLC) was necessary to confirm which product was the star polymer and which the linear polymer. However, by using an initiator containing porphyrin, the separation of the star polymer was achieved by means of HPLC with a variable-wavelength UV detector, and thus we could optimize the polymerization conditions for selective synthesis of star aromatic polyamides. Furthermore, there are rather few reports on the synthesis of porphyrin-cored star polymers with rigid arms, as compared with star polymers with flexible-coil polymer arms.4 For example, porphyrin-cored star polyfluorenes was synthesized by Sun and co-workers by self-polycondensation of benzoxazine homocyclic ester in the presence of a porphyrin core having four 1,1-difluorosuccinimide moieties. In this polymerization, the length of the arms was not controlled and the molecular weight distribution was broad.5 Therefore, not only the synthesis, but also the properties of porphyrin-cored star polymers with well-defined rigid or semirigid arms remain to be fully established.

In this article, we investigated the chain-growth condensation polymerization of 4-tolylaminobenzonic acid ester 1 with porphyrin-cored tetra-functional initiator 3 under various conditions and optimized the conditions for selective synthesis of star-shaped poly(p-benzamide) with suppression of the formation of linear self-condensed polyamides (Scheme 1).

EXPERIMENTAL

Materials

Commercially available dehydrated tetrahydrofuran (stabilizer-free, Kanto) was used as a dry solvent.

Tetrakis(4-carboxyphenyl)porphine (TCEP, TCI), zinc(II) acetate dihydrate (Aldrich), lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, 1.0 M solution in THF, Aldrich) were used as received. 18-Crown-6 (TCI) was used after drying overnight under reduced pressure at 32 °C/hexane = 3/1) to obtain a purple solid (78%, m.p. 90-92 °C). Most star polymers with controlled molecular weight and low polydispersity are synthesized by living polymerization, a kind of living polymerization yielding condensation polymerization, the length of the arms was not controlled and the molecular weight distribution was broad.6 Therefore, not only the synthesis, but also the properties of porphyrin-cored star polymers with well-defined rigid or semirigid arms remain to be fully established.

Synthesis of Initiator 3

Tetrakis(4-carboxyphenyl)porphine (TCEP, TCI), zinc(II) acetate dihydrate (Aldrich), lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, 1.0 M solution in THF, Aldrich) were used as received. 18-Crown-6 (TCI) was used after drying overnight under reduced pressure at 32 °C/hexane = 3/1) to obtain a purple solid (78%, m.p. 90-92 °C). Most star polymers with controlled molecular weight and low polydispersity are synthesized by living polymerization, a kind of living polymerization yielding condensation polymerization, the length of the arms was not controlled and the molecular weight distribution was broad.6 Therefore, not only the synthesis, but also the properties of porphyrin-cored star polymers with well-defined rigid or semirigid arms remain to be fully established.

Materials

Commercially available dehydrated tetrahydrofuran (stabilizer-free, Kanto) was used as a dry solvent.
Table 1. Polymerization of Ib with 3

| Entry | N   | Temp. (°C) | Conv. (%) | $M_n$, onset | $M_n$, circ | $M_n$, nom. | $M_w/M_n$ |
|-------+-----+-----------+-----------+-------------+-------------+-------------+-----------|
| 1     | 80  | -10       | 95        | 19,700      | 9,500       | 18,600      | 1.33      |
| 2     | 80  | -10       | 95        | 20,500      | 10,100      | 20,000      | 1.35      |
| 3     | 81  | -10       | 100       | 20,600      | 15,200      | 22,800      | 1.07      |
| 4     | 80  | -10       | 100       | 20,500      | 15,600      | 24,700      | 1.09      |
| 5     | 38.5| 10        | 100       | 11,000      | 10,700      | 11,900      | 1.05      |
| 6     | 120.4| 10       | 100      | 29,600      | 22,200      | 22,700      | 1.11      |
| 7     | 158.5| 10       | 100      | 38,400      | 20,600      | 47,900      | 1.20      |

*Polymerization of Ib with 3 was carried out in the presence of 1.0 equivalent of LiHMDS in THF (10h).*

* Determined by HPLC.
* Determined by GPC based on polystyrene standards (aden: THF).

Table 2. Polymerization of 1b with 3

| Entry | N   | Temp. (°C) | Conv. (%) | $M_n$, onset | $M_n$, circ | $M_n$, nom. | $M_w/M_n$ |
|-------+-----+-----------+-----------+-------------+-------------+-------------+-----------|
| 1     | 80  | -10       | 95        | 19,700      | 9,500       | 18,600      | 1.33      |
| 2     | 80  | -10       | 95        | 20,500      | 10,100      | 20,000      | 1.35      |
| 3     | 81  | -10       | 100       | 20,600      | 15,200      | 22,800      | 1.07      |
| 4     | 80  | -10       | 100       | 20,500      | 15,600      | 24,700      | 1.09      |
| 5     | 38.5| 10        | 100       | 11,000      | 10,700      | 11,900      | 1.05      |
| 6     | 120.4| 10       | 100      | 29,600      | 22,200      | 22,700      | 1.11      |
| 7     | 158.5| 10       | 100      | 38,400      | 20,600      | 47,900      | 1.20      |