Macromolecules **1999,** *32,* 6881−6884 **6881**

A New Approach to Hyperbranched Polymers by Ring-Opening Polymerization of an AB Monomer: 4-(2-Hydroxyethyl)-ϵ-caprolactone

Mingjun Liu, Nikolay Vladimirov, and Jean M. J. Fréchet*

Department of Chemistry, University of California, Berkeley, California 94720-1460

Received May 18, 1999
Revised Manuscript Received August 19, 1999

The concept of hyperbranched polymers was first presented in theoretical work by Flory in 1952.[1] However, it did not attract interest until 1988 when the first example of this type of macromolecule was reported by Kim and Webster.[2] Since then, there has been much interest in this area,[3] and a large number of hyperbranched polymers have been reported based on a variety of different chemical architectures including, for example, polyesters,[4] polyethers,[5] polyamides,[6] polyphenylenes,[7] polyurethanes,[8] polysiloxysilanes,[9] and others.[10] Meanwhile, some of the physical properties of hyperbranched polymers have also been investigated.[3]

A majority of hyperbranched polymers reported to date have been prepared by step-growth polymerization of AB_2-type monomers. We have also reported recently the novel proton-transfer polymerization of AB_2 epoxy monomers[11] and the "self-condensing vinyl polymerization" (SCVP) of functionalized vinyl monomers.[12] A variety of AB vinyl monomers have now been reported to undergo SCVP to give hyperbranched polymers by cationic,[12] free radical,[13] or group transfer polymerization.[14] The use of ring-opening polymerization has also been reported for the preparation of hyperbranched polymers.[3a,15,16] In a recent review, Kim mentioned briefly the attempted ring-opening polymerization of 2-hydroxylmethyloxetane under basic conditions, a sluggish reaction that failed to produce a hyperbranched polyether.[3a] In contrast, Suzuki et al. used the Pd-catalyzed ring-opening polymerization of a cyclic carbamate in the presence of an initiator to afford a branched polyamine.[15]

Here we present a new approach to the preparation of hyperbranched polymers that combines ring-opening polymerization and some of the features found in SCVP. This new approach was demonstrated by polymerization of monomer **1** as shown in Scheme 1. Monomer **1** contains both an ϵ-caprolactone ring that is well-known to polymerize by ring-opening polymerization and a primary alcohol group that may initiate the ring-opening polymerization of ϵ-caprolactone under certain activation conditions (110 °C, stannous octoate as catalyst). Despite the lack of a vinyl group, this monomer has some analogies to those used in SCVP; that is, it is an AB monomer containing one polymerizable group and one initiating moiety. The polymerization process is initiated by the ring opening of the ϵ-caprolactone group of one AB monomer with one initiating alcohol group of another monomer, affording a dimer **2** with one ϵ-caprolactone group and two primary alcohol groups. Therefore, the AB monomer **1** has effectively been transformed into an AB_2-type monomer that is well-known to polymerize to afford hyperbranched macromolecules. Additional ring-opening steps involving monomer **1** and dimer **2** result in larger oligomers. Eventually high molecular weight hyperbranched macromolecules **3** are produced by subsequent condensation of increasingly larger oligomers. Unlike other preparation of hyperbranched polymers by ring-opening polymerization, this reaction proceeds entirely through one type of reactive nucleophile: a primary alcohol.

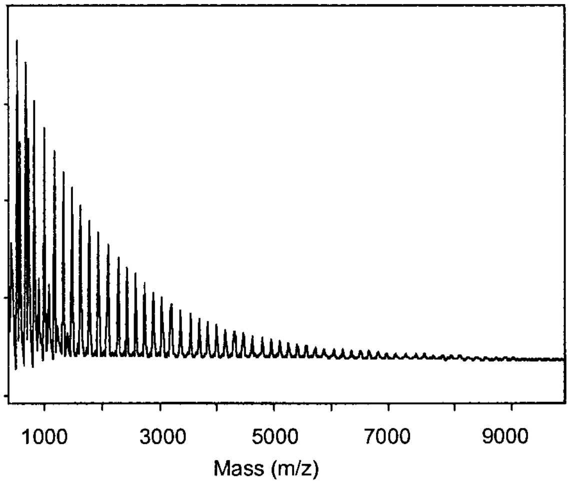


Figure 1. MALDI-TOF MS spectrum of polymer **3**.

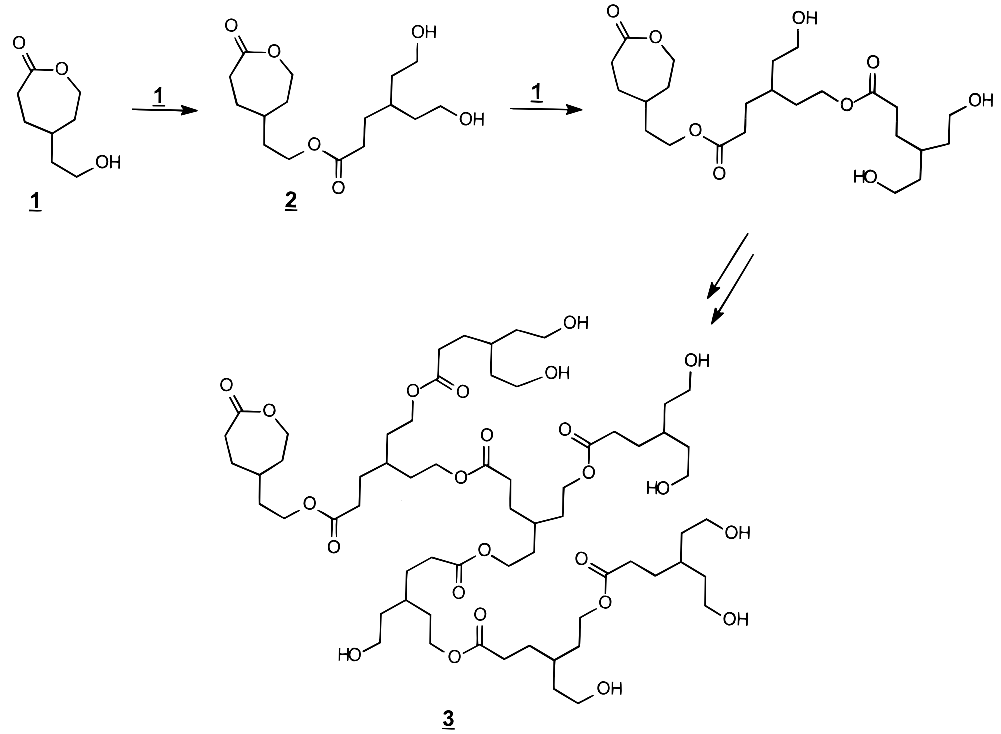
The preparation of monomer **1** is shown in Scheme 2. The starting compound **4** was prepared according to a literature procedure.[17] Protection of the hydroxyl group of **4** with benzyl group, followed by deprotection of the acetal group, afforded **5** in 88% yield. Ketone **5** was then converted to the corresponding ester **6** in 98% yield via the Baeyer−Villiger oxidation.[18] Finally, removal of the benzyl protecting groups by hydrogenolysis afforded the desired monomer **1** in quantitative yield as a clear liquid.

Bulk polymerization of **1** was carried out at 110 °C in the presence of a catalytic amount of stannous octoate.[19] The polymerization process was monitored closely by size exclusion chromatography (SEC). In the early stage, a gradual buildup of dimers, trimers, tetramers, and higher oligomers is observed. As the reaction proceeds, the concentration of the lower oligomers decreases while higher molecular weight polymer is formed. The kinetics of the ring-opening polymerization process was studied using different amounts of catalyst. As expected, the amount of catalyst has a great influence on the rate of polymerization. In the presence of 1 mol % of catalyst, the polymerization was complete in 1 h, while the reaction was slower at lower catalyst concentrations. An interesting feature observed in the kinetic study is that after rising rapidly the molecular weight of polymer reaches a maximum and then remains constant. Once the maximum is reached, a longer reaction time does not lead to a further increase of molecular weight or to the formation of insoluble materials. Presumably, this is due to the consumption of ϵ-caprolactone ring by intramolecular macrocyclization reactions.

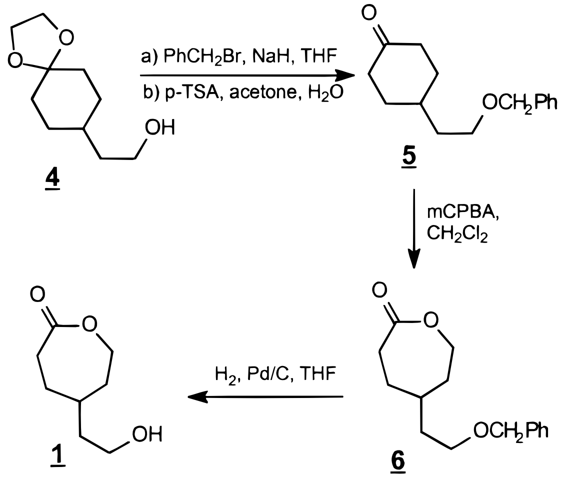
Hyperbranched polymer **3** is a clear viscous liquid that may easily be obtained with M_w in the range 65 000−85 000 and with a polydispersity of ca. 3.2 (as measured by SEC in DMF with polystyrene standards). The molecular weight varies with the concentration of

10.1021/ma990785x CCC: $18.00

Scheme 1



Scheme 2



catalyst, and lower catalyst concentrations tend to give polymers with higher molecular weights. Polyester **3** with its large number of alcohol end groups is soluble in polar solvents, such as DMSO, DMF, and methanol, but insoluble in THF, CH_2Cl_2, and $CHCl_3$.

Figure 1 shows the MALDI-TOF MS spectrum of a sample of hyperbranched polyester **3**. A series of peaks with spacing of 158 mass unit (corresponding to the molecular weight of the monomer) were detected from MW 340 to ca. 10 000. These peaks correspond to the sodium adducts of the dimer to the 63-mer. The peak intensity for these oligomers decreased sharply as the molecular weight increased. This is not surprising since the higher oligomers and all polyesters with MW > 10 000 may not fly well under the conditions used for this analysis and therefore cannot be detected. The proposed structure of the hyperbranched polyesters was also confirmed by ^{1}H and ^{13}C NMR spectroscopy.

The degree of branching (DB) of hyperbranched polymers as originally defined by Hawker, Lee, and Fréchet[4a] is expressed as

$$\mathrm{DB} = \frac{(\text{no. of dendritic units}) + (\text{no. of terminal units})}{\text{total no. of units}}$$

Both ^{1}H NMR and ^{13}C NMR have been utilized to determine DB.[4a,c] Examination of the structure of polymer **3** reveals that four different types of subunits A, B, C, and D may be present as shown in Figure 2. It is most likely that subunit A at the focal point is not present as a result of the intramolecular reaction described above. Even if it were present, its molar proportion would be so low that it could be ignored without affecting significantly the DB calculation. Subunit B represents the terminal unit with two alcohol groups, subunit C is the linear unit with one alcohol group and one ester group, and finally subunit D is the dendritic unit with two ester groups and no alcohol

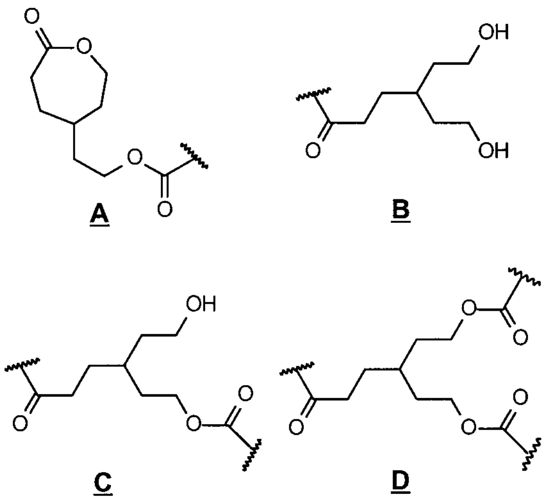


Figure 2. Structure of possible subunits in polymer **3**.

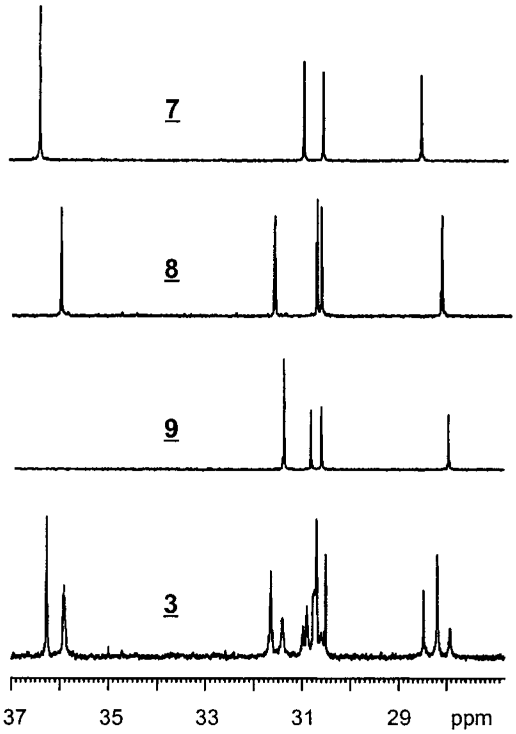
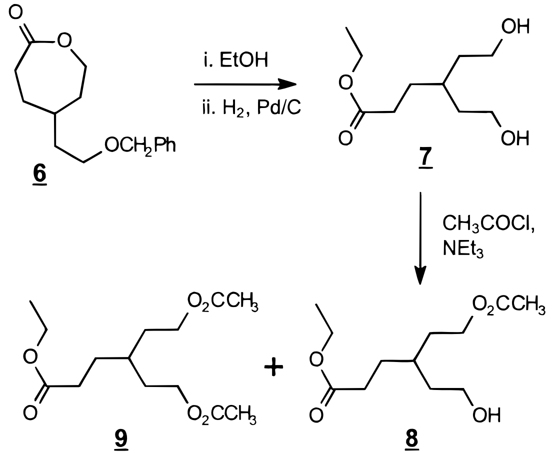


Figure 3. The 500 MHz ^{13}C NMR spectra for model compounds and polymer **3** in DMSO-d_6.

Scheme 3



group. The ^{13}C NMR spectrum of **3** exhibits much fine structure related to its branching pattern that may be used to determine the DB. To facilitate the assignment, three model compounds representing the subunit B, C, and D were prepared as shown in Scheme 3. The ^{13}C NMR spectra of these compounds, as well as that of polymer **3**, are shown in Figure 3. As can be seen from these spectra, all related ^{13}C resonances of the model compounds are also found in the spectrum of polymer **3**, and some of these are well-resolved. These resonances can easily be assigned to the different subunit B, C, and D by a simple comparison with those of the model compounds. The DB of hyperbranched polyester **3** calculated from the relative integration of the various ^{13}C signals was determined to be 0.50.

The presence of a large number of alcohol groups at the chain ends allows further surface modification reactions. To demonstrate this, a simple end-capping reaction was performed using acetyl chloride in the presence of triethylamine to afford polyester **3a** with acylated end groups. The complete extent of the acylation reaction was confirmed by ^1H NMR, which shows both the completed disappearance of the alcohol protons and the appearance of methyl protons. The solubility of the hyperbranched polyester changes dramatically upon acylation of its alcohol chain ends. After acylation, polyester **3a** is still soluble in DMF and DMSO; it also becomes soluble in THF, CH_2Cl_2, and $CHCl_3$ but is no longer soluble in methanol.

In conclusion, we have demonstrated a new approach to a hyperbranched polyester. The resulting hyperbranched polyester consists of the building block of poly(ϵ-caprolactone) that are known to be biodegradable and biocompatible.[20] Since the aliphatic polyesters, such as poly(ϵ-caprolactone) and poly(lactide), are widely used in biomedical applications, the new hyperbranched polyesters may find uses in similar applications. In addition, the large number of chain ends may offer these hyperbranched polyesters other advantages compared with the case of linear poly(ϵ-caprolactone); for example, these functional groups may be used to attached biologically active molecules. The biodegradability of these new hyperbranched polyesters is currently under investigation.

Acknowledgment. Funding of this research by the National Science Foundation (DMR 9816166) and the US Army Research Office (MURI program DAAG55-97-0126) is gratefully acknowledged.

References and Notes

(1) Flory, P. J. *J. Am. Chem. Soc.* **1952**, *74*, 2718.

(2) (a) Kim, Y. H.; Webster, O. W. *ACS Polym. Prepr.* **1988**, *29* (2), 310. (b) Kim, Y. H.; Webster, O. W. *J. Am. Chem. Soc.* **1990**, *112*, 4592.

(3) For recent reviews, see: (a) Kim, Y. H. *J. Polym. Sci., Polym. Chem.* **1998**, *36*, 1685. (b) Malmstrom, E.; Hult, A. *J. Macromol. Sci., Rev. Macromol. Chem. Phys.* **1997**, *C37*, 555. (c) Fréchet, J. M. J.; Hawker, C. J. In *Comprehensive Polymer Science*, 2nd Supplement; Aggarwal, S. L., Rosso, S., Eds.; Pergamon Press: London, 1996; p 71. (d) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendritic Macromolecules: Concepts, Syntheses, Perspectives*; VCH: Weinheim, Germany, 1996. (e) Voit, B. I. *Acta Polym.* **1995**, *46*, 87. (f) Fréchet, J. M. J.; Hawker, C. J. *React. Polym.* **1995**, *26*, 127.

(4) (a) Hawker, C. J.; Lee, R.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4583. (b) Turner, S. R.; Voit, B. I.; Mourey, T. H. *Macromolecules* **1993**, *26*, 4617. (c) Malmstrom, E.; Johansson, M.; Hult, A. *Macromolecules* **1995**, *28*, 1698. (d) Trollsås, M.; Atthoff, B.; Claesson, H.; Hedrick, J. L. *Macromolecules* **1998**, *31*, 3439. (e) Trollsås, M.; Hedrick, J. L. *Macromolecules* **1998**, *31*, 4390.

(5) (a) Uhrich, K. E.; Hawker, C. J.; Fréchet, J. M. J.; Turner, S. R. *Macromolecules* **1992**, *25*, 4583. (b) Miller, T. M.; Neenan, T. X.; Kwock, E. W.; Stein, S. M. *J. Am. Chem. Soc.* **1993**, *115*, 356. (c) Percec, V.; Kawasumi, M. *Macromolecules* **1992**, *25*, 3843.

(6) (a) Uhrich, K. E.; Boegeman, S.; Fréchet, J. M. J.; Turner, S. R. *Polym. Bull.* **1991**, *25*, 551. (b) Kim, Y. H. *Adv. Mater.* **1992**, *4*, 764.

(7) Kim, Y. H.; Webster, O. W. *Macromolecules* **1992**, *25*, 5561.

(8) Spindler, R.; Fréchet, J. M. J. *Macromolecules* **1993**, *26*, 4809.

(9) (a) Mathias, L. J.; Carothers, T. W. *J. Am. Chem. Soc.* **1991**, *113*, 4043. (b) Miravet, J. F.; Fréchet, J. M. J. *Macromolecules* **1998**, *31*, 3461.

(10) van Benthem, R. A. T. M.; Muscat, D.; Stanssens, D. A. W. *Polym. Mater. Sci. Eng.* **1999**, *80*, 72.

(11) Chang, H. T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1999**, *121*, 2313.

(12) Fréchet, J. M. J.; Henmi, M.; Gitsov, I.; Aoshima, S.; Leduc, M. R.; Grubbs, R. B. *Science* **1995**, *269*, 1080.

(13) (a) Hawker, C. J.; Fréchet, J. M. J.; Grubbs, R. B.; Dao, J. *J. Am. Chem. Soc.* **1995**, *117*, 10763. (b) Gaynor, S. G.; Edelman, S.; Matyjaszewski, K. *Macromolecules* **1996**, *29*,

1979. (c) Weimer, M. W.; Fréchet, J. M. J.; Gitsov, I. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 955.
(14) (a) Sakamoto, K.; Aimiya, T.; Kira, M. *Chem. Lett.* **1997**, 1245. (b) Simon, P. F. W.; Radke, W.; Müller, A. H. E. *Polym. Prepr.* **1997**, *38*, 498. (c) Simon, P. F. W.; Radke, W.; Müller, A. H. E. *Macromol. Rapid Commun.* **1997**, *18*, 865.
(15) (a) Suzuki, M.; Ii, A.; Saegusa, T. *Macromolecules* **1992**, *25*, 7071. (b) Suzuki, M.; Yoshida, S.; Shiraga, K.; Saegusa, T. *Macromolecules* **1998**, *31*, 1716.
(16) After this paper was submitted, a report was published which describes the synthesis of hyperbranched polyglycerols by ring-opening multibranching polymerization. See: Sunder, A.; Hanselmann, R.; Frey, H.; Mülhaupt, R. *Macromolecules* **1999**, *32*, 4240.
(17) Ciufolini, M. A.; Byrne, N. E. *J. Am. Chem. Soc.* **1991**, *113*, 8016.
(18) Krow, G. R. *Org. React.* **1993**, *43*, 251.
(19) (a) Trollsas, M.; Hedrick, J. L.; Mecerreyes, D.; Dubois, Ph.; Jerome, R.; Ihre. H.; Hult, A. *Macromolecules* **1998**, *31*, 2756. (b) In't Veld, P. J. A.; Velner, E. M.; Van DeWhite, P.; Hamhuis, J.; Dijkstra, P. J.; Feijen, J. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 219.
(20) Pitt, C. G. In *Biodegradable Polymers as Drug Delivery Systems*; Chasin, M., Langer, R., Eds.; Marcel Dekker: New York, 1990; p 71.

MA990785X