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NATURAL AND SYNTHETIC UNIFORM POLYMERS

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ABSTRACT

Uniformity of polymer structure is discussed in regard of natural and synthetic uniform polymers. Natural uniform polymers such as enzyme proteins and nucleic acids are uniform with respect to molecular weight, chemical structure, monomer sequence, stereoregularity, and conformation (shape). These kinds of uniformity give rise to their highly specific functions (uniform function) as catalysis by enzyme and genetic replication by DNA. Synthetic uniform polymers that have uniform molecular weight and chemical structure have proved useful in fundamental studies in polymer science. Recent advances in separation technology have provided a means of separating synthetic uniform polymers from its homologous mixture. The method has more general applicability and provides uniform polymers as a series of homologs which are useful for systematic studies on the nature of polymers. The example of this is discussed for uniform poly(methyl methacrylate) (PMMA). End-functionalized uniform PMMAs were also obtained by chromatographic separation and used to construct such uniform polymer architectures as star, block, and comb polymers.

INTRODUCTION

Uniform polymer has been defined in an IUPAC document as "a polymer composed of molecules uniform with respect to relative molecular mass and constitution" [1]. The "relative molar mass" is practically identical with molecular weight.

The "constitution" means chemical structure such as monomeric unit and end group. Thus, a polyethylene comprises the following polymer molecules of the same molecular weight is not a uniform polymer:

$$CH_3\text{-}(CH_2\text{-}CH_2)_{100}\text{-}CH_2\text{-}CH{=}CH_2 \quad \text{and} \quad CH_3\text{-}(CH_2\text{-}CH_2)_{100}\text{-}CH{=}CH\text{-}CH_3$$

The IUPAC definition does not regard the uniformity in stereochemical configuration (stereoregularity) and conformation (shape). One can define such a uniformity by adding an appropriate adjective; a stereoregular uniform polymer and conformationally uniform polymer.

When Nature creates a molecule with sophisticated functions, she designs and produces a uniform polymer, such as protein for catalysis and nucleic acid for replication, which are uniform with respect to molecular weight, sequence arrangement of constitutional units, configuration (stereoregularity), and conformation or shape. If we look into natural polymers as a model for the macromolecular design of polymeric materials, such a high level uniformity should also be considered.

Recent advances in polymer chemistry have provided opportunity of controlling molecular weight of polymers via living polymerizations in a variety of mechanisms [2]. Although polymers with a narrow molecular weight distribution (MWD) obtained by living polymerization are often faultily called uniform or monodisperse, they definitely have molecular weight distribution with a limit of polydispersity index ($\overline{M}_w/\overline{M}_n$) given by Poisson distribution [3]; for a given degree of polymerization (DP), $\overline{M}_w/\overline{M}_n = DP/(DP + 1)$. The nonuniformity of synthetic narrow MWD polymers, which has been hidden in a conventional GPC analysis, has recently been revealed by several analytical means such as MALD-TOF (matrix-assisted laser-desorption time-of-flight) mass spectrometry [4] and supercritical fluid chromatography (SFC) [5–9]. It is worth noting that the terms "uniform polymer" and "nonuniform polymer" are recommended to replace the widely used but nondescriptive and self-contradictory terms "monodisperse polymer" and "polydisperse polymer" [10].

EARLY ATTEMPTS IN UNIFORM POLYMERS

Before the concept of "hochmolekularen Verbindungen" was established by Staudinger, Fischer prepared an oligopeptide comprising regularly sequenced 15 glycine (G) and 3 leucine (L) units: L-G-G-G-L-G-G-G-L-G-G-G-G-G-G-G-G-G, which is an early example of a chemically synthesized uniform oligomer [11].

During his struggle to establish the macromolecular concept, Staudinger attempted to obtain uniform oligo(oxymethylene) diacetates with DP ranging from 1 to 26 [12]. Each uniform oligomer was separated by careful solvent fractionation and recrystallization and confirmed by chemical analysis and molecular weight measurement. Even though a recent investigation [13] on the same type of oligomers purified by SFC fractionation revealed that the melting points reported by Staudinger were a little lower than the recently reported values, there is no doubt that Staudinger's data have been of great importance for establishing the existence of macromolecules.

PREPARATION OF SYNTHETIC UNIFORM POLYMERS

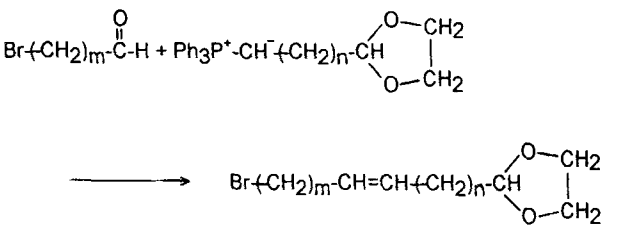
Methods for the preparation of uniform polymers may be categorized as follows:

1. Chemical synthesis
2. Genetic engineering
3. Chromatographic separation

Other methods such as the topochemical approach are also discussed in a recent review [9].

1. Chemical Synthesis of Uniform Polymers

The highest DP synthetic uniform polymer ever made is polymethylene (or polyethylene in a conventional name): $C_{390}H_{782}$, DP as polyethylene being 195. The principal step in the synthesis involves a coupling between ω-bromoalkanal and a Wittig reagent derived therefrom:



A series of uniform polymethylenes have been used successfully to investigate the lamella crystal structure of polyethylene [14]. Other examples of the synthesis of uniform polymers include poly(oxyethylene)s [15], dendrimers [16], and polypeptides [17]. The synthesis of uniform poly(oxyethylene) involves coupling between α,ω-ditosylate and the monosodium salt of an 18mer of ethylene oxide. The dendrimers are known to take a spherical shape and are potentially useful for the control of shape uniformity. The final step of dendrimer synthesis via the convergent method [16] involves coupling dendritic segment molecules with a polyfunctional core. Uniform polypeptides are now routinely synthesized by a solid-phase peptide synthesizer. For example, interleukin-8 (comprising 72 residues) can be obtained in the amount of 27 mg in 5 days [17].

2. Genetically Engineered Uniform Polypeptide

The uniform polypeptide synthesis recently developed by Tirrell's group [18–20] utilizes the genetic engineering for the de novo design of the peptide sequence as well as the length of the polypeptide, and, as a consequence of this precise structural control, allows the control of three-dimensional alignment of the peptide chains.

3. Chromatographic Separation

Besides these synthetic means, separation techniques such as HPLC have provided versatile tools for the separation of uniform polymers. Uniform cyclopoly(dimethylsilylene) with DP up to 16 can be isolated by HPLC [21]. SFC has proved more powerful for the separation of polymers or higher DP oligomers [5–9]. In 1978, Klesper and Hartmann reported the SFC fractionation of styrene oligomers up to octamer, while a chromatogram shown in the literature indicates that separation was attained up to 50mer, though the elution from dimer to 50mer took about 16–17 hours [6]. The instrumental development in SFC technology, combined with improved column efficiency, now provides a better separation of a polystyrene sample of the same DP range within half an hour [22], making the SFC fractionation of a uniform polymer more practical.

STEREOREGULAR UNIFORM PMMA

Besides the control of molecular weight of polymers enabled by living polymerizations [2], another concern in the precise synthesis of polymer is the control of stereoregularity, the importance of which was pointed out earlier by Staudinger [23] and realized later by Natta [24] by the invention of isotactic polyolefins. Recently we reported stereospecific and living polymerizations of methacrylate which afford highly isotactic [25], syndiotactic [26], and heterotactic [27] polymers with narrow MWD. Figure 1(a) shows an SFC chromatogram of an isotactic poly(methyl methacrylate) (PMMA) obtained by the isotactic living polymerization with

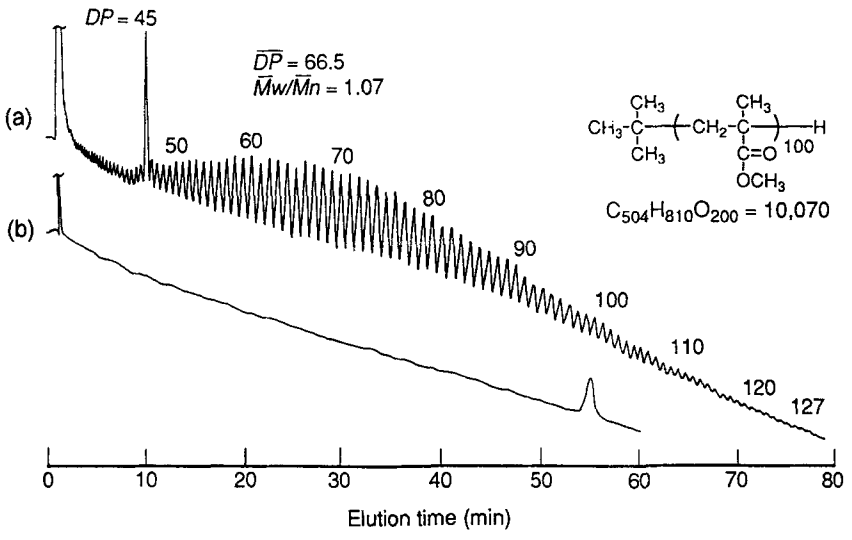


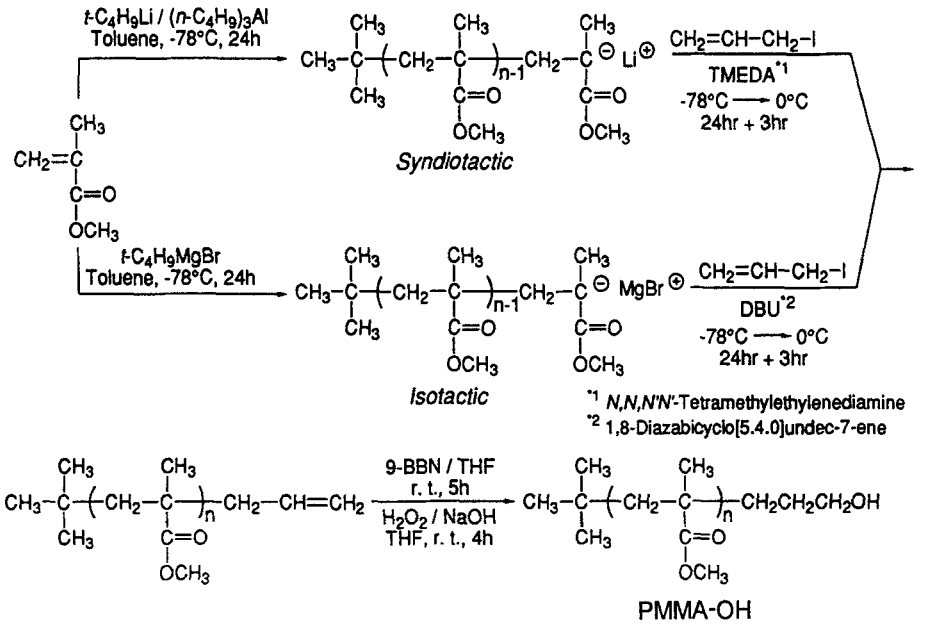
FIG. 1. SFC traces of isotactic PMMA (DP = 66.5, M_w/M_n = 1.07, *mm:mr:rr* = 97.7:2.3:0.0) containing an authentic sample of the 45mer (a) and of the isolated 100 mer (b) [8]. Mobile phase: CO_2, 12.0 mL/min; CH_3OH, 2.8 mL/min; column, silica gel, 10 mm i.d. × 250 mm; temperature: 80→40°C; pressure: 240 kg/cm^2; sample loaded: 25 mg.

$\overline{DP}$ of 66.5 and $\overline{M}_w/\overline{M}_n$ of 1.07, consisting of almost 105 components of a homologous series of isotactic PMMA. By applying this chromatography to the separation of the mixture into each component, it is now possible to obtain synthetic uniform PMMAs with DP up to 100 (Fig. 1b) [7-9]. Uniform polymers are pure model substances of polymers and, as expected, exhibit higher crystallinity than the corresponding nonuniform polymers [28] and are suitable for structural studies of polymers. Melting points and glass transition temperatures of a series of uniform isotactic and syndiotactic PMMAs were determined, and the molecular weight dependencies of these properties were definitely obtained [22]. These uniform polymers are also useful as a molecular weight standard in GPC analysis [7] and for investigating the process of stereocomplex formation between isotactic and syndiotactic PMMAs in solution by means of GPC [7].

UNIFORM POLYMER ARCHITECTURE VIA COMBINATION OF LIVING POLYMERIZATION TECHNIQUE AND SFC SEPARATION

A synthetic merit of living polymerization is to afford end-functionalization of polymers, which are useful for the construction of a variety of macromolecular architectures [2]. Combining this synthetic advantage of living polymerization and the high efficiency of separation given by the SFC technique, we recently obtained end-functionalized uniform PMMAs and utilized them as uniform building blocks to construct uniform polymer architectures such as block, star, and comb polymers.

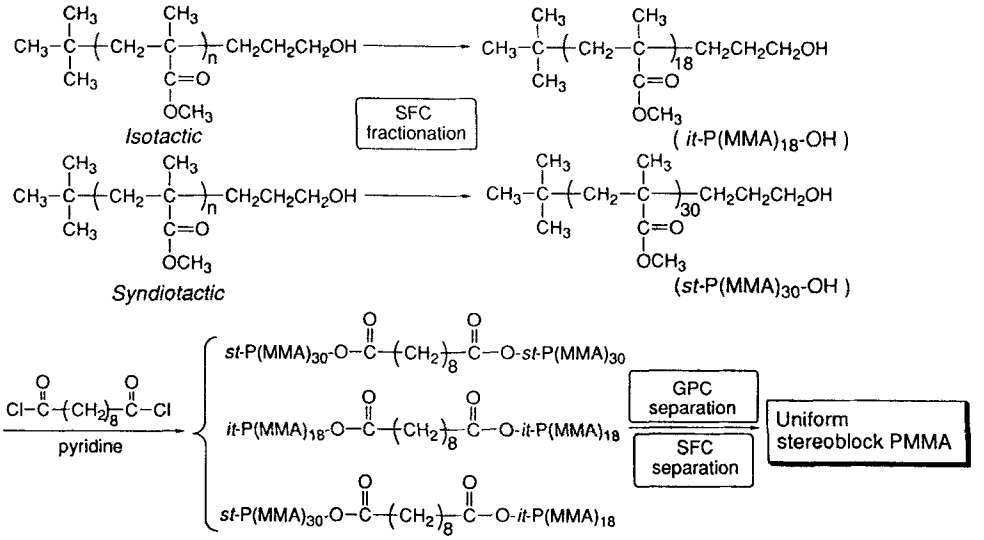
Scheme 1 illustrates the synthesis of stereoregular PMMAs having a hydroxy group at one end (PMMA-OH) [29]. The isotactic and syndiotactic PMMA-OH



SCHEME 1. Preparation of hydroxy-terminated syndiotactic and isotactic PMMAs.

were fractionated by SFC into each uniform PMMA-OH [30]. The terminal OH group provides a handle to prepare a block copolymer by a condensative coupling with dicarboxylic acid chloride. The coupling reaction of isotactic PMMA-OH (DP = 18) and syndiotactic PMMA-OH (DP = 30) with sebacyl chloride was carried out in toluene in the presence of pyridine at room temperature (see Scheme 2). The product contained three types of coupled products, isotactic-isotactic (*it-it*), syndiotactic-syndiotactic (*st-st*), and isotactic-syndiotactic (*it-st*). The difference in DP of the starting uniform polymers resulted in the difference in the DP of these products, *it-it* (36), *st-st* (60), and *it-st* (48), and thus facilitated the separation of the cross-coupled product (*it-st*), a stereoblock uniform PMMA, from the others by means of GPC and SFC. The stereoblock uniform PMMA formed a stereocomplex when annealed at 90°C for 48 hours; the melting point of the complex was 106.9°C with the ΔH for the melting of the complex being 0.95 cal/g. The mixture of the corresponding uniform PMMAs showed a melting point of 103.9°C with a ΔH of 0.39 cal/g. The higher melting point and larger ΔH for the stereoblock uniform PMMA clearly indicate that the chemical linkage between isotactic and syndiotactic PMMA chains facilitates the association of the stereoregular chain segments. The minimum DP required for the complex formation will be clarified in the near future by using a series of uniform stereoblock PMMAs of different DPs. The enhancement of complexation ability by linking the two PMMA segments has been demonstrated by using non-uniform stereoblock PMMA prepared by a living polymerization [31]. However, information on the minimum DP is obtainable only with the aid of the uniform stereoblock PMMA.

The syndiotactic uniform PMMA-OH (DP = 26) has also been used to prepare uniform star polymer through the reaction with benzenetricarboxylic acid chloride to give a uniform three-armed star polymer [32]. Though the reaction product contained mono-armed, di-armed, and tri-armed uniform polymers besides the un-

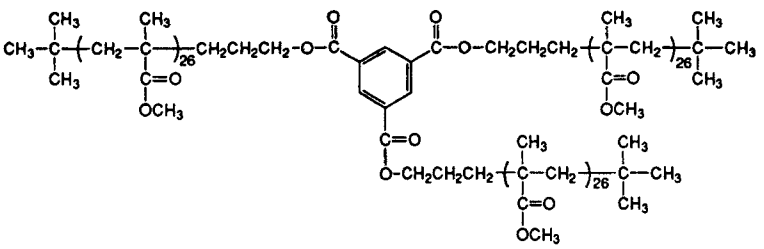


SCHEME 2. Preparation of uniform stereoblock PMMA.

reacted PMMA-OH, each component could easily be separated by GPC owing to the uniformity of the arm length. Figure 2 shows GPC curves of the products of the coupling reaction of benzenetricarboxylic acid chloride with uniform and nonuniform PMMA-OHs. It is apparently difficult to separate tri-armed star polymer from the nonuniform products.

The branching effect on viscosity behavior is one of the main subjects in the study of star polymer. Plots of $\log[\eta]$ against log MW, according to Mark-Houwink-Sakurada's equation, indicate clearly that the plot for the tri-armed uniform star polymer deviates from the linear extrapolation of the plots for the mono- and di-armed polymers, which are linear chains. The results demonstrate the effect of branching on the viscosity without ambiguity.

PMMA macromonomers with methacryloyl group as a polymerizable function have been prepared from PMMA-OH [33].



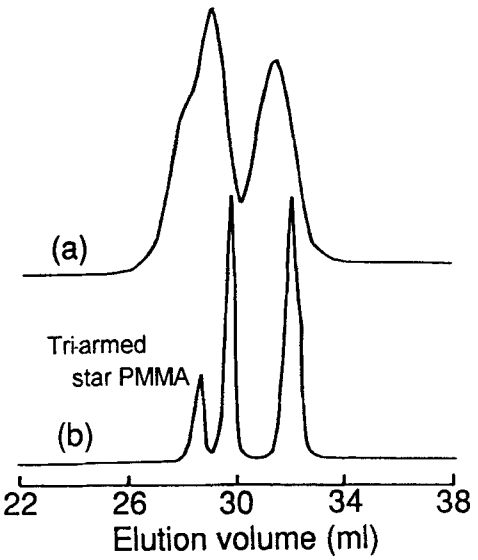
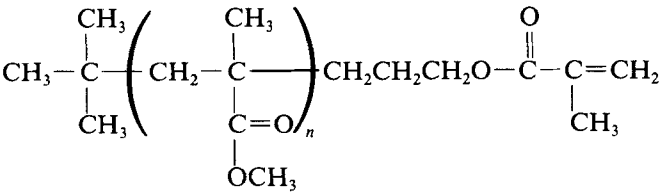


FIG. 2. GPC curves of the reaction mixture of benzenetricarboxylic acid chloride and syndiotactic PMMA-OH in the presence of pyridine in toluene. (a) Nonuniform PMMA-OH ($\overline{DP}$ = 32.7, $\overline{M}_w/\overline{M}_n$ = 1.04). (b) Uniform PMMA-OH (DP = 26). The structure of tri-armed star polymer is shown at the top.



The syndiotactic PMMA macromonomer was separated by SFC into the uniform macromonomers. Radical polymerization of the uniform PMMA macromonomer (DP = 28) was carried out in benzene at 60°C with AIBN, giving a comblike polymer with uniform side-chains. On the contrary, if the non-uniform macromonomer, even with narrow MWD as Poisson distribution, is polymerized, macromonomers of different DPs should be incorporated into each polymacromonomer molecule, that is, the polymerization is actually a multicomponent copolymerization, resulting in a wide range of composition of the product. As a result, the molecular weight of each individual polymacromonomer molecule cannot be related directly to the number of branch. Moreover, the main-chain DP has also a distribution. Thus, theoretical modeling of such a complex system seems almost impossible or meaningless. The polymacromonomer obtained from the uniform macromonomer is exactly a homopolymer and, accordingly, should be a very useful material for studies on the nature of comb polymer, even though the main-chain DP has a distribution.

Fractionation of the oligo(macromonomer) by GPC gives uniform comblike oligomers with DP in the main chain up to 4. Due to the low DP, these uniform oligo(macromonomer)s exhibited a $\log[\eta]$–log MW relationship similar to those for the uniform star polymer.

The above examples demonstrate the use of end-functionalized uniform polymers for the construction of more complex polymer structures. These methods also provide higher molecular weight uniform polymers which are difficult to obtain by separation.

NATURAL UNIFORM POLYMER VS SYNTHETIC UNIFORM POLYMER

As mentioned in the Introduction, some natural polymers, such as enzymes and nucleic acids, have extremely high levels of uniformity not only in their primary and tertiary structures but also in their functions (Fig. 3). The IUPACs definition

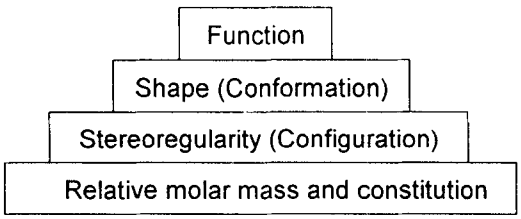


FIG. 3. Hierarchy of uniformity in macromolecular architecture. IUPAC's definition: A polymer which is uniform with respect to its relative molar mass and constitution.

of uniform polymer only describes the lowest level of uniformity, molecular weight, and constitution. As described in this paper, our synthetic uniform PMMA stays at this level, though the uniformity in stereoregularity is partly realized. The higher level of uniformity has not been achieved.

Natural uniform polymers are of perpetual interest because of their sophisticated functions. For these specific functions, they are made so purposely that their structures seem to be very distinctive among polymer molecules in general.

The preparation of uniform polymers by means of chromatographic separation has the advantage that the method provides uniform polymers with a continuous series of DP. Natural uniform polymers are never obtained in such a way; for example, a series polyalanine of different DP may not exist in Nature, and would be useless for biological activity. Block, graft, star, and comb polymers of uniform chain lengths are rarely found in Nature, but we can prepare them by the combination of synthetic approach and chromatographic separation. The synthetic uniform polymers thus obtained are unique in this regard and will be useful in systematic studies for the fundamental understanding of the nature of chain molecules in general.

In conclusion, natural uniform polymers are highly uniform in every way and display their functions as a molecule, which is one of the ultimate goals of macromolecular design. In a broader aspect of polymer science, however, synthetic uniform polymers are also important for deepening our knowledge of polymer science and leading to a more generalized theory of polymers as chain molecules. Though it is still difficult to provide large quantities of synthetic uniform polymers, it is evident that our knowledge of polymer science will be profoundly extended through studies of uniform polymers.

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REFERENCES

[1] IUPAC, *Compendium of Macromolecular Nomenclature*, Blackwell Science Publishers, 1991, p. 52.
[2] O. W. Webster, *Science, 251*, 887 (1991).
[3] P. J. Flory, *J. Am. Chem. Soc., 62*, 1561 (1940).
[4] P. O. Danis and D. E. Karr, *Org. Mass Spectrom., 28*, 923 (1993).
[5] M. Saito (Ed.), *Fractionation by Packed-Column SFC and SFE*, VCH Publishers, New York, NY, 1994.
[6] E. Klesper and W. Hartmann, *Eur. Polym. J., 14*, 77 (1978).
[7] K. Ute, N. Miyatake, Y. Osugi, and K. Hatada, *Polym. J., 25*, 1153 (1993).

[8] K. Hatada, K. Ute, T. Kitayama, T. Nishiura, and N. Miyatake, *Macromol. Symp., 85*, 325 (1994).
[9] K. Hatada, K. Ute, and N. Miyatake, *Prog. Polym. Sci., 19*, 1067 (1994).
[10] IUPAC, "Definitions of Terms Relating to Individual Macromolecules, Their Assemblies, and Dilute Polymer Solutions," *Pure Appl. Chem., 61*, 211 (1989).
[11] E. Fischer, *Chem. Ber., 40*, 1754 (1907).
[12] H. Staudinger, H. Johner, R. Signer, G. Mie, and J. Hengstenberg, *Z. Phys. Chem., 126*, 425 (1927).
[13] K. Ute, T. Takahashi, K. Matsui, and K. Hatada, *Polym. J., 25*, 1275 (1993).
[14] G. Ungar, J. Stejny, A. Keller, I. Bidd, and M. C. Whiting, *Science, 229*, 386 (1985).
[15] S. Kinugasa, A. Takatsu, H. Nakanishi, H. Nakahara, and S. Hattori, *Macromolecules, 25*, 4848 (1992).
[16] C. J. Hawker and J. M. J. Fréchet, *J. Am. Chem. Soc., 112*, 7638 (1990).
[17] I. Clark-Lewis, B. Moser, A. Walz, M. Baggiolini, G. J. Scott, and R. Aebersold, *Biochemistry, 30*, 3128 (1991).
[18] K. P. McGrath, M. J. Fournier, T. L. Mason, and D. A. Tirrell, *J. Am. Chem. Soc., 114*, 727 (1992).
[19] E. Yoshikawa, M. J. Fournier, T. L. Mason, and D. A. Tirrell, *Macromolecules, 27*, 5471 (1994).
[20] J. G. Tirrell, M. Fournier, T. L. Mason, and D. A. Tirrell, *Chem. Eng. News*, p. 40 (December 19, 1994).
[21] L. F. Brough, K. Matsumura, and R. West, *Angew. Chem., Int. Ed. Engl., 18*, 955 (1979).
[22] K. Ute and K. Hatada, *Preprints, 3rd Pacific Polymer Conference, Gold Coast (Australia)*, December 13–17, 1993, p. 479.
[23] H. Staudinger, A. A. Ashclown, M. Brunner, H. A. Bruson, and S. Wehrli, *Helv. Chim. Acta, 12*, 934 (1929).
[24] G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mazzanti, and G. Moraglio, *J. Am. Chem. Soc., 77*, 1708 (1955).
[25] K. Hatada, K. Ute, K. Tanaka, Y. Okamoto, and T. Kitayama, *Polym. J., 18*, 1037 (1986).
[26] T. Kitayama, T. Shinozaki, T. Sakamoto, M. Yamamoto, and K. Hatada, *Makromol. Chem. Suppl., 15*, 167 (1989).
[27] T. Kitayama, Y. Zhang, and K. Hatada, *Polym. J., 26*, 868 (1994).
[28] K. Ute, N. Miyatake, and K. Hatada, *Polymer, 36*, 1415 (1995).
[29] T. Kityamama, O. Nakagawa, S. Kishiro, T. Nishiura, and K. Hatada, *Polym. J., 25*, 707 (1993).
[30] K. Hatada, T. Nishiura, T. Kitayama, K. Ute, and S. Hirotani, *Ibid.*, Submitted.
[31] T. Kitayama, N. Fujimoto, T. Yanagida, and K. Hatada, *Polym. Int., 33*, 165 (1994).
[32] K. Hatada, T. Nishiura, T. Kitayama, and M. Tsubota, *Polym. Bull., 36*, 399 (1996).
[33] K. Hatada, T. Nishiura, T. Kitayama, and S. Hirotani, To Be Submitted to *Polym. J.*