Star Poly(ethylene oxide)s from Carbosilane Dendrimers†

B. Comanita, B. Noren, and J. Roovers*

National Research Council of Canada, Institute for Chemical Process and Environmental Technology, Ottawa, Ontario, Canada K1A 0R6

Received July 31, 1998; Revised Manuscript Received December 1, 1998

ABSTRACT: A series of 4-arm, 8-arm, and 16-arm poly(ethylene oxide)s (PEO) have been synthesized from hydroxy functionalized carbosilane dendrimers of generation zero, one, and two, respectively. The PEO arms are grown anionically from the multifunctional cores. The polymers have narrow molecular weight distributions. Analysis of the molecular weight, intrinsic viscosity, and translational diffusion coefficient in methanol confirms the star structure of the polymers. The aqueous solutions of the star PEOs appear normal. Low molecular weight star polymers, however, show abnormally low intrinsic viscosities and are adsorbed on the size exclusion column hydrogel material.

Introduction

Poly(ethylene glycol) and poly(ethylene oxide) (PEO) have interesting biological properties.[1,2] Star-branched poly(ethylene oxide)s are expected to provide additional potential in a variety of biomedical applications.[3,4] The methods for making PEO stars are limited. In the arm-first method preformed monofunctional PEO chains are coupled to multifunctional coupling agents. Smid et al. coupled hydroxy terminated PEO to multifunctional isocyanates.[5] Recently, this method was expanded to the coupling of 32 PEO chains (MW = 5000) onto a third-generation poly(amidoamine) dendrimer.[6] The original hydroxy end group of the polymer was first reacted with succinic anhydride, and the resulting carboxylic acid was activated with *N*-hydroxysuccinimide for the reaction with the end-standing primary amines of the dendrimer. Coupling to dendrimers of higher functionality led to reduced incorporation of PEO arms. Star PEOs have also been produced by the radical polymerization of ω-hydroxy PEO macromonomers.[7] The method is also limited to low MW PEO, and the product has a wide molecular weight distribution. Extremely high MW stars are obtained when the macromonomer is polymerized in water. PEO macromonomers with end-standing norbornene groups have recently been polymerized by ring-opening metathesis catalyst.[8] In principle, this method leads to narrow MWD materials.

The core-first method involves the living polymerization of ethylene oxide from a multifunctional initiator. This has traditionally been accomplished by anionic initiation with a poly(divinylbenzene) living core or from a poly(styryl-*b*-divinylbenzene) living core.[9,10] The PEO star polymers have narrow MWD arms. However, the number of arms is difficult to control and, probably, has a fairly wide distribution. Furthermore, the resulting star polymers have a large weight fraction of hydrocarbon material that makes them unsuitable for biomedical applications.[11]

In this report we describe the synthesis of star PEOs starting from multifunctional carbosilane dendrimers. The number of arms and the MW of each PEO arm are strictly controlled. Furthermore, each arm has an end-standing hydroxy group which is available for further modification. The method expands on the work of Taton and Gnanou, who prepared a six-arm PEO starting from a heptaphenyl core.[12] The polymers are characterized by their dilute solution properties.

† NRCC Publication No. 41980.

Experimental Section

Synthesis. The synthesis of the carbosilane dendrimer core[13] and the modification required for the attachment of end-standing hydroxy groups[14] have been described. All further operations are performed under high vacuum with additions through fragile break-seals. The multifunctional initiator and the cryptate, kryptofix [2,2,2], are extensively dried under high vacuum. EO is purified by degassing and stirring over CaH_2 and two films of Na that were prepared by vacuum distillation. The solvent, THF, is purified by distillation from CaH_2 and treatment with Na/K alloy to the characteristic blue color. The reaction vessel is pumped and dried under high vacuum, and THF is distilled in. The initiator, potassium naphthalene, and the cryptate are added in that order. Then purified EO is distilled between −30 and 0 °C. The reaction flask is warmed to 25−30 °C with stirring. After several hours the solution becomes clear. The polymerization is then completed at 40 °C. The polymerization time essentially depends on the potassium concentration. The reaction is terminated with a drop of glacial acetic acid, and the polymer is precipitated in hexane, dried, and stored under vacuum in the dark. Linear reference PEOs are made in the same way starting from purified *tert*-butyl alcohol.

Characterization. Linear and star PEOs are characterized by SEC in THF at 35 °C. Adsorption of the polymers on the columns is prevented by the addition of 0.25% $(n\text{-Bu})_4NBr$ to THF.[15] The flow rate is 1 mL/min. Ultrastyragel columns (Waters) with nominal pore size 10^5, 10^4, and 10^3 are used with DRI and UV detectors. Commercial narrow MWD PEO samples (Polymer Laboratories) are used to verify the chromatographic system. All polymers have also been analyzed by SEC in water at 35 °C. Three Ultrahydrogel columns (Waters) 1000, 500, and 250 were used. The flow rate is 0.5 mL/min with a DRI detector and 18-crown-6 as an internal standard.

All polymer solutions are prepared overnight in the dark at 35−40 °C. Methanol was fractionally distilled from CH_3ONa under N_2. Weight-average MWs are determined in methanol at 25 °C with a Brookhaven BI30 instrument. Five solutions are prepared and clarified by filtration through 0.2 μm nylon filters.[16] The Rayleigh ratio for toluene at 633 nm, equal to 1.4×10^{-5} cm^{-1}, is the calibrating constant. $dn/dc = 0.135$ mL/g was determined on three high molecular weight PEO samples and is in agreement with ref 17. The MWs are obtained from Berry plots. Dynamic light scattering measurements are made on the same solutions. Autocorrelation results are collected in 256 channels. The diffusion coefficient is extracted by means of the method of cumulants. Second cumulant results are retained. No angular dependence of the diffusion constant is observed. The concentration dependence used to extrapolate to zero concentration is of the form $D = D_0(1 + k_D c)$. The viscosity and density of methanol are 0.544 cP and 0.7865 g/cm^3, respectively. Viscosities are measured in methanol

10.1021/ma981201e CCC: $18.00 Published 1999 by the American Chemical Society
Published on Web 01/29/1999

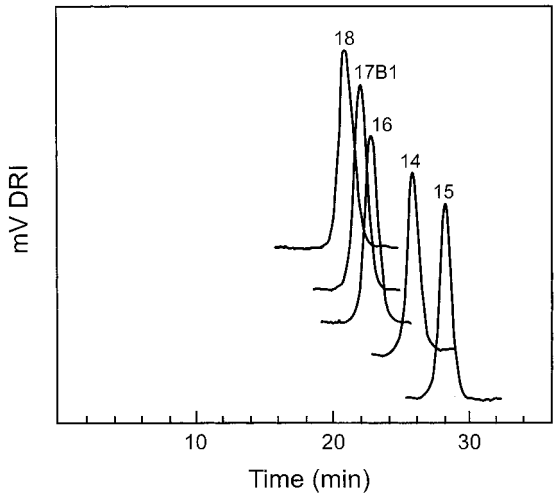

Figure 1. SEC profiles of 4-arm star PEOs. Conditions: THF, 0.5% (n-Bu)$_4$NBr, 35 °C, 1 mL/min, DRI.

at 25 °C and in water (18 MΩ cm) at 35 °C with semi-micro Cannon Ubbelohde viscometers. The solvent flow times are 185 and 197 s, respectively. Aqueous solutions of star PEOs showed considerable foaming, making accurate measurements more difficult. Huggins and Kraemer plots are used to obtain the intrinsic viscosity.

Results and Discussion

The synthesis of the star PEOs is shown schematically by

$$\left.\begin{array}{l}\\ \text{Si - (CH}_2\text{)}_6\text{OK}\\ \\ \end{array}\right] + \text{n EO} \rightarrow \left.\begin{array}{l}\\ \text{Si - (CH}_2\text{)}_6\text{ - (OCH}_2\text{CH}_2\text{)}_n\text{ - OK}\\ \\ \end{array}\right]$$

where the large bracket at silicon indicates that the silicon atom is connected to a carbosilane dendrimer with several such functional groups. The hydroxy-modified carbosilane dendrimers are sparingly soluble in THF. Partial substitution with potassium decreases the solubility further even in the presence of solubilizing cryptate. The initial polymerization is therefore performed at 25 °C with stirring. The potassium counterion concentration is smaller than the hydroxy concentration. A fast dynamic equilibrium between alkoxide and hydroxy groups ensures narrow MWD of all the PEO arms.[18,19] The polymers have narrow MWD as evidenced by their SEC traces in THF and in water as shown in Figure 1. Uncorrected apparent MWD are between 1.05 and 1.08. Occasionally, traces of low MW material are observed. These are thought to originate from spurious water or methanol, two reagents that are difficult to remove completely from the initiator. In some cases, the low molecular weight material (≈5%) has been removed by fractional separation in benzene/hexanes at 35 °C following the method of Booth and Price.[20]

The molecular characteristics of the linear and star PEOs are summarized in Table 1. The MW of the star PEO can be estimated from the ^{1}H NMR spectrum when the MW is not very high. For example, the ratio of the Si−CH$_2$ protons at 0.43 ppm to the CH$_2$−CH$_2$−O protons at 3.60 ppm indicates that the degree of polymerization per arm is 32.5 in PEO-15. The total MW of PEO-15, including the initiator fragment, is therefore 6130.

The MW of high MW samples are determined by static light scattering in methanol at 25 °C. The measurements lead to satisfactory Berry plots. The molecular weights of linear reference samples agree well with the manufacturer's values. The molecular weights of the star polymers agree with the stoichiometry of the polymerization. It is noted, however, that the values of A_2 of the linear polymers (see Table 1) are about 2.5 times lower than the values derived from ref 17. They are in fair agreement with the data of Kinugasa.[21] Earlier literature on association phenomena of PEO in water and methanol have been reviewed.[16,22] Although we have no experimental evidence for association, it is nevertheless felt that both solvents cause some problems of reproducibility. The data obtained with the linear PEO samples in methanol and water are used as the benchmark data for the study of the star PEO samples.

In methanol, the slopes of double-logarithmic plots of $[\eta]$ against MW are given by 0.707 ± 0.01. See Table 2. These slopes are substantially larger than that obtained by Zhou (0.585),[17] and they identify methanol as a good solvent for PEO. An average value of 0.70_7 was used to calculate the prefactors of the Mark−Houwink−Sakurada relation for each polymer architecture.

$$[\eta] = K^* M_w^{0.707} \text{ (mL/g)} \quad (1)$$

Values of K are summarized in Table 2. The shrinkage factor $g' = [\eta]/[\eta]_l$ is derived for the three types of star polymers. The numerical values of g' differ slightly from those quoted earlier, based on $a = 0.69_5$.[23] The shrinkage factors are in excellent agreement with those of nonpolar star polymers in good organic solvents.[24,25] These results indicate that PEO and the PEO star polymers are swollen random coils in methanol and that the dendritic core has no significant effect on the polymer conformation.

The PEO polymers presently available are too small for an accurate determination of their radius of gyration by static light scattering. However, dynamic light scattering in methanol at 25 °C provides translational diffusion coefficients. See Table 1. The double logarithmic plots of D_0 vs M_w yield a slope $a_f = -0.56_7$ for linear PEO. The values for the star polymers are given in Table 3. From the Mark−Houwink−Sakurada exponent one expects $a_f = -1/2 - [(a - 1/2)/3] = -0.56_9$. The prefactors in $D_0 = K_f M_w^{-a_f}$ for linear PEO and the stars with 4, 8, and 16 arms are given in Table 3 together with the hydrodynamic shrinkage factors $g_h = D_{0,l}/D_0 = R_h/R_{h,1}$. The values of g_h for the different star polymers are also in good agreement with those of model nonpolar polymers in nonpolar solvents.[24,25] The hydrodynamic radii calculated by

$$R_h = kT/(6\pi\eta_s D_0) \quad (2)$$

are shown in Figure 2. The viscometric radii calculated by

$$R_\eta = \left(\frac{3}{10\pi N_A}[\eta]M\right)^{1/3} \quad (3)$$

reveal that $R_\eta = 1.20R_h$ for linear PEO and that R_η/R_h decreases with increasing branching.

Intrinsic viscosities have also been measured in water at 35 °C, i.e., near body temperature. The data are collected in Table 1 and shown in Figure 3. It is first noted that values of $[\eta]$ in water are slightly higher than in methanol for linear PEOs. The slope in Figure 3 is 0.71_6, slightly higher than in methanol. Several recent

Table 1. Characteristics of Linear and Star PEOs

sample	$M_w \times 10^{-4}$	$M_w{}^a/M_n$	$A_2 \times 10^3$ mL/g	$D_0 \times 10^7$(cm^2/s) (methanol, 30 °C)	[η] (mL/g) (methanol, 30 °C)	[η] (mL/g) (water, 35 °C)	R_η/R_h
linear PEO							
PEG23k	2.46	1.15	1.04	10.0	30.9	36.0	1.23
BC1PEO20k	(2.7)	1.11			32.7	37.4	
BC1PEO100k	(9.4)	1.14			84.6	99.0	
PEO160k	16.7	1.09	0.91	3.2	118	$137._5$	1.16
PEO293k	27.7	1.16	0.97	2.4_6	$173._5$	$204._5$	1.21
4-arm star PEO							
PEO15	0.61[b]	1.07					
PEO14	2.19	1.06	1.14	11.1_5	20.9	21.4	1.15
PEO16	10.5	1.07	0.70	4.5	62.9	73.2	1.14
PEO17B1	17.8	1.06	0.61	3.3_6	93.0	$106._0$	1.16
PEO18B2	32.8	1.09	0.55	2.37	142.0	$165._0$	1.15
8-arm star PEO							
BC8PEO2k	2.04[c]	1.08	0.79	13.0	12.9_5	12.0	1.12
BC8PEO8k	8.5_1	1.07	0.62	6.0_3	35.0	35.4	1.17
BC8PEO25kB1	15.0	1.06	0.55	4.28	51.4	56.2	1.14
BC8PEO60kB4	45.7	1.08	0.42	2.26	$111._4$	$132._8$	1.13
16-arm star PEO							
BC16PEO2kF1	4.8[d]	1.06		9.2	13.5	13.1	1.03
BC16PEO6k	14.2	1.07	0.35	5.23	28.4	31.7	1.12
BC16PEO5k	19.2	1.09	0.26	4.0_8	36.2	39.0	1.05
BC16PEO16k	32.6	1.07	0.33	3.1_6	52.4	58.6	1.10

[a] By SEC in THF. [b] M_n by ^{1}NMR. [c] $M_n = 1.9 \times 10^4$ by ^{1}NMR. [d] $M_n = 5.0 \times 10^4$ by ^{1}NMR.

Table 2. Molecular Weight Dependence of Intrinsic Viscosity of PEO

	methanol			water		
	a	$K^a \times 10^{2\,a}$	g′	a	$K^a \times 10^{2\,b}$	g'
linear	0.70_7	2.45_5		0.71_6	2.55_5	
4-arm	0.70_8	1.79	0.72_8	0.75_4	1.85	0.72_7
8-arm	0.69_3	1.13_6	0.46_3	0.75_9	1.11	0.43_5
16-arm	0.71_8	0.66_0	0.26_9	0.78_3	0.64	0.25_1

[a] Calculated with $a = 0.707$. [b] Calculated with $a = 0.716$; see text for justification.

Table 3. Molecular Weight Dependence of Translational Diffusion Coefficients of PEO in Methanol

	a_f	$K_f \times 10^{4\,a}$	g_h
linear	-0.56_7	2.98	
4-arm	-0.56_7	3.20	0.93_3
8-arm	-0.56_0	3.62	0.82_4
16-arm	-0.56_4	4.07	0.73_3

[a] Calculated with $a_f = -0.567$.

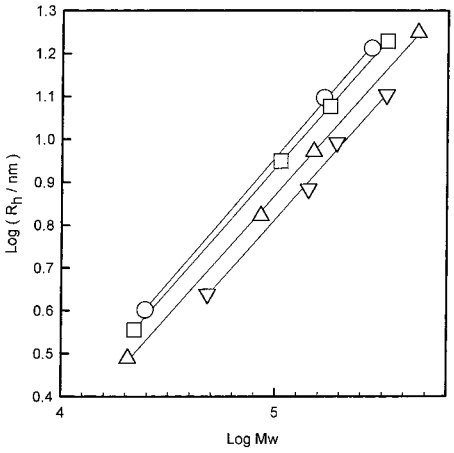

Figure 2. Hydrodynamic radii versus molecular weight in methanol at 25 °C. Symbols: linear, ○; 4-arm, □; 8-arm, △; and 16-arm star PEO, ▽.

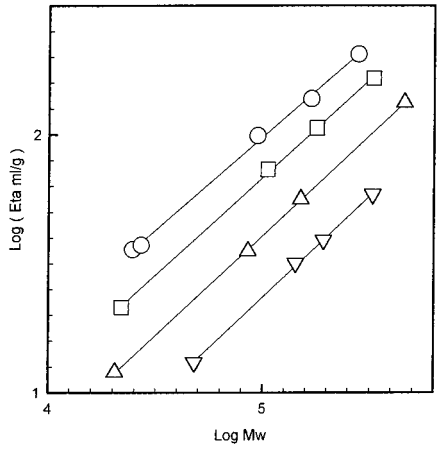

Figure 3. Intrinsic viscosity vs molecular weight in water at 35 °C. Symbols as in Figure 2.

reports have provided Mark−Houwink−Sakurada relations for PEO in water.[26−28] Different exponents, 0.657,[26] 0.679,[27] and 0.791,[28] are quoted for results obtained at 25 and 30 °C over different MW ranges. Despite this wide range of exponents, fairly good agreement on the actual intrinsic viscosities emerges for all data, including ours, in the MW range 2×10^4 to 10^6.

The Mark−Houwink−Sakurada exponents for the star PEOs in water are shown in Table 2. In contrast with the behavior in methanol, the exponents increase with increasing functionality of the stars. Closer inspection of the values of [η] in water and comparison with the data in methanol reveals that this increased MW dependence is entirely due to the low values of [η] of low MW star PEOs and that high MW star PEOs have intrinsic viscosities in water that are consistent with those of the linear polymers. To analyze the intrinsic viscosities of the star polymers in water, only the high MW results are considered. The values of the prefactors of the Mark−Houwink−Sakurada relations calculated with a constant exponent $a = 0.71_6$ are collected in Table 2. The shrinkage ratios in water, also shown in Table 2, appear slightly smaller than in methanol. Similar small differences have been observed also in nonpolar star polybutadienes in cyclohexane and toluene, two equally good solvents.[29] The shrinkage factors provide indirect proof that the stars have monodisperse arms. Indeed, if the arms would have a most probable distri-

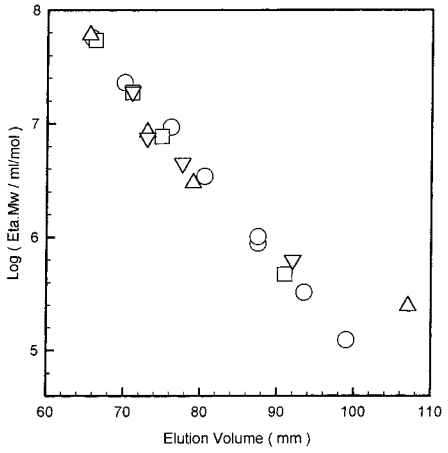

Figure 4. Universal calibration for linear, 4-arm, 8-arm, and 16-arm star PEO. SEC in water at 35 °C, 0.5 mL/min, DRI detector. Symbols as in Figure 2.

bution, then g, the shrinkage factor for the radius of gyration, would be given by $g = 6f/(f + 1)^2$ rather than $g = (3f - 2)/f^2$ for regular stars.[30] Since $g' \approx g^{1/2}$ for low functionality stars in good solvents, much increased values of g' would result in the case of stars with polydisperse arms. This was observed experimentally by Schaefgen and Flory in the case of polyester star polymers.[31]

At this point we have no good explanation for the low viscosities of samples BC8PE02k and BC16PEO2k in water. Molecular mechanics calculations on the second-generation carbosilane dendrimer (16-hydroxy groups) indicate that the distance between the central Si and its peripheral oxygens is about 13 Å.[32] The value of R_h of BC16PEO2k in methanol is 47 Å. The PEO corona is therefore only 34 Å thick. The size exclusion chromatography data obtained for the linear, 4-, 8-, and 16-arm star polymers are shown in the universal calibration form (log $[\eta]M_w$ vs elution volume) in Figure 4. Although there is some scatter, a single curve is obtained. Deviations to longer elution volumes are observed for the smallest 8-arm and smallest 16-arm star polymers. The former with $M_{arm} = 2500$ deviates more than the latter with $M_{arm} = 3000$. Both samples have a broad elution profile in water with substantial tailing. This appears to be evidence that the PEO arms of these low MW polymers do not sufficiently screen the hydrophobic core and thereby allow some interaction of the core with the column material.

Conclusion

It has been shown that 4-, 8-, and 16-arm star PEOs can be prepared in a controlled way from multifunctional hydroxy modified carbosilane dendrimers. The anionic polymerization provides simultaneous growth of all arms and yields narrow MW distribution polymers. Characterization of the star polymers and comparison of the properties with those of linear PEO indicate that the core material has a minimal effect on the conformation of the stars in methanol. In water, however, PEO star polymers with small arms ($M_{arm} \leq$ 3000) seem to be slightly collapsed. Adsorption of these polymers on the hydrogel of the SEC column was also observed. When the MW of the PEO arms is large, no such abnormal behavior is found. The molecular weight at which PEO screens the carbosilane core cannot presently be determined for lack of a larger number of samples.

Acknowledgment. The authors thank Dr. P. Peng and Mr. L. Lazare for technical help at the early stages of this research. We thank Prof. N. Hadjichristidis for the refractive index increment measurements. Financial support from Organogel Canada Ltée and the NRC-NSERC Collaborative Research Program is acknowledged.

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MA981201E