Preparation and Characterization of Pure Oligo(ethylene glycol)s. 2

Shinichi Kinugasa,* Akiko Takatsu, Hiroshi Nakanishi, Hisae Nakahara, and Shigeru Hattori

National Chemical Laboratory for Industry, Higashi, Tsukuba 305, Japan

Received February 11, 1992; Revised Manuscript Received May 1, 1992

ABSTRACT: A pure sample of an oligo(ethylene glycol) (OEG), tetrapentaconta(ethylene glycol) (HO-$(CH_2CH_2O)_{54}H$ (OEG54)), has been prepared by stepwise synthesis coupled with preparative size exclusion chromatography (SEC) used as a separation method. The purity of the OEG54 sample has been checked by analytical SEC and differential scanning calorimetry. Furthermore, the molecular weights (MW) of the OEG54 sample and a pure sample of octadeca(ethylene glycol) (OEG18) previously prepared have been determined by mass spectroscopy, light scattering (LS), vapor pressure osmometry, ^{13}C NMR, and ^1H NMR. The observed MW values of the OEG samples are in good agreement with those expected from their chemical formulas. In particular, fairly good agreements observed in LS and ^1H NMR measurements show that these pure OEG samples can be used as ideal MW standard samples.

Introduction

Since Bömer et al.'s pioneering work,[1] various pure oligomers of ethylene glycol (OEGx, where x is the degree of polymerization in $HO(CH_2CH_2O)_xH$) have been prepared by Booth and co-workers:[2] these pure samples are prepared by stepwise synthesis coupled with preparative size exclusion chromatography (SEC) used as a purification method. They have been used as model polymers for crystallographic and calorimetric studies of poly(ethylene oxide) (PEO).[3]

These oligomeric samples are important not only as model compounds but also as standard reference materials for molecular weight determination because they have definite molecular weight values expected from their chemical formulas. For example, in light scattering (LS) measurements, one can successfully use these pure samples for calibrating LS instruments and determining absolute scattered light intensities. Furthermore, they may be more favorably used as standard samples for calibrating other characterization methods such as SEC and vapor pressure osmometry (VPO) than commercial poly(ethylene glycol) (PEG) standard samples.

Characterization of these pure OEG samples has been carried out by various methods: SEC,[1,2,4] mass spectroscopy (MS),[2a,b] ^1H NMR,[2] IR,[2] VPO,[2a] LS,[5] and Raman spectroscopy.[6] However, only a few quantitative measurements to determine their molecular weights M or degree of polymerization x have been performed successfully for low-molecular-weight OEGs.[5] For high-molecular-weight OEGs, the values of M or x have been speculated only from chromatographic peak positions in their SEC chromatograms. Hence, it is interesting and important to determine their M or x by different characterization techniques.

For oligomers, various techniques for molecular weight determination have been used. LS is an advantageous technique for determining the weight-average molecular weight M_w of not only polymers but also oligomeric compounds of low molecular weight: even the molecular weights of simple organic liquids ($M \sim 100$) can successfully be determined by this technique.[7] On the other hand, VPO has been widely used for obtaining the number-average molecular weight M_n for various oligomers, including PEGs.[8,9] Moreover, spectroscopic methods such as ^1H NMR are also available for such oligomers having at least one characteristic chemical group at their terminal ends. For example, recent ^1H NMR experiments[10] on commercial PEG samples using deuterated dimethyl sulfoxide (DMSO-d_6) as solvent have shown that their molecular weights can be successfully determined from the ratio between the signal of the terminal hydroxy (OH) protons and that of the CH_2CH_2O backbone protons.

These pure OEG samples can be used as primary standards for molecular weight determination. In fact, low-molecular-weight compounds are ideal substances for determining absolute intensities in LS measurements.[11] If adequate excess scattered light intensities would be expected from the oligomeric solutions, the value of the Rayleigh ratio R_B of pure benzene could readily be determined by comparing the scattered intensity from benzene with that from these pure OEG samples.

Additionally, the OEG samples can also be used in adjusting characterization instruments. For example, optimum values for various instrumental conditions or parameters such as the number of data points in recent NMR measurements could be easily and precisely adjusted with the help of the samples.

In our previous study,[5,12] we prepared OEG18 on the basis of Booth et al.'s procedure and determined its molecular weight by LS. A good agreement between the measured molecular weight and that calculated from its chemical formula showed that it can be used as a molecular weight standard.

To extend our studies, we have prepared pure OEG54 with 54 oxyethylene units according to a modified procedure which is similar to that reported in our previous paper.[5,12] Additionally, the molecular weights of both OEG18 and OEG54 have been determined by LS, VPO, ^{13}C NMR, and ^1H NMR. We have also estimated the accuracy or the limit of errors in measurements of these experimental methods by comparing measured molecular weights and those expected from their chemical formulas.

Experimental Section

Preparation of Pure OEG54. Pure OEG18 was prepared and purified as described in our previous papers.[5,12] Pyridine, p-toluenesulfonyl chloride (TsCl), dichloromethane, and tetrahydrofuran (THF) were purified by almost the same procedures as described in Teo et al.'s study.[2b] Prior to use, reagent grade sodium hydride (NaH) (Wako Chemicals, Japan) dispersed in

* To whom correspondence should be addressed.

0024-9297/92/2225-4848$03.00/0

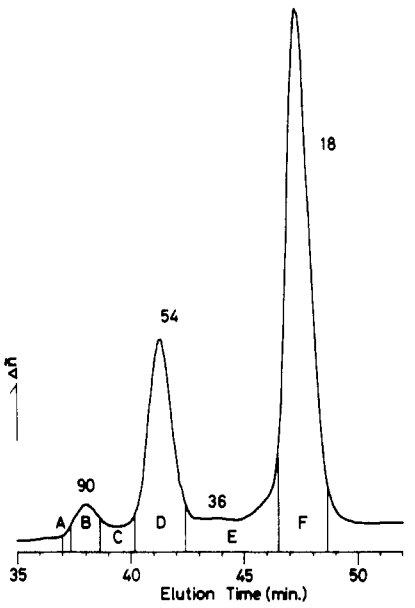

Figure 1. Preparative SEC chromatogram of the oligomeric mixture. Separation conditions are as follows: columns, TSKgel-G3000H$_6$ (5.5 cm i.d. × 60 cm) × 2; flow rate, 40 mL·min^{-1}; eluent, THF; injection of the sample, 0.63 g in 16 mL of THF. Numbers on the peaks represent degree of polymerization.

oil was washed with dry *n*-hexane in a glass funnel under dry nitrogen (N_2).

Under dry N_2, a solution of TsCl (1.22 g, 6.40 × 10^{-3} mol) in dry pyridine (4.4 mL) was added to a solution of OEG18 (1.00 g, 1.23 × 10^{-3} mol) in dry pyridine (7.8 mL) cooled at −30 °C. The reaction mixture was stirred under dry N_2 at −30 °C for a week. The resultant mixture was then poured rapidly into ice and water (52 mL, vigorously stirred) and then stirred for 4 h. The mixture was then extracted with dichloromethane (8.5 mL × 8). The dichloromethane solution was washed with hydrochloric acid (6 mol·L^{-1}, 11 mL × 3), aqueous ammonium chloride (saturated, 7 mL × 1), and distilled water (5 mL × 3) and then dried with anhydrous sodium sulfate (Na_2SO_4). The solution was filtered and concentrated by rotary evaporation. Yield: 1.01 g (73%). The IR (NaCl) and ^{1}H NMR ($CDCl_3$) spectra of the product were consistent with its expected chemical structure. Elemental analysis: Calcd for OEG18 ditosylate ($C_{50}H_{86}O_{23}S_2$): C, 53.65; H, 7.74; S, 5.73. Found: C, 53.25; H, 7.74; S, 5.49. Analytical SEC showed no peak corresponding to the monotosylate of OEG18.

An oligomeric glycol mixture was synthesized as follows: A solution of OEG18 (5.05 g, 6.23 × 10^{-3} mol) in THF (11 mL) was added to a solution of sodium hydride (0.07 g, 2.9 × 10^{-3} mol) in THF (10 mL) stirred under dry N_2 at room temperature. After bubbling of hydrogen ceased, the reaction mixture (yellow solution) was stirred for 30 min. To this stirred solution was added a solution of OEG18 ditosylate (1.01 g, 9.02 × 10^{-4} mol) in THF (7.5 mL). The flask was then shielded from light, and the reaction mixture was stirred at room temperature for 10 days. After the white precipitate of sodium tosylate (NaOTs) was filtered off with a glass funnel, THF was evaporated and then a clear yellow liquid, which crystallized on standing, was obtained. Distilled water (11.5 mL) was added to the residue, and the aqueous liquid was gently refluxed for 3 h. The aqueous solution was brought to pH ≃ 7 with HCl (2 mol·L^{-1}) and then extracted with dichloromethane (6.6 mL × 10). The organic extract was washed with sodium carbonate (10%, 1.4 mL × 1), and the aqueous washing was reextracted with dichloromethane (3.5 mL × 5). Finally, the combined organic extract was washed with distilled water (1 mL × 2) and dried (Na_2SO_4), and the dichloromethane was evaporated to yield a mixture of oligomeric glycols (5.07 g).

OEG54 was separated from the oligomeric glycol mixture by preparative high-performance SEC under the following conditions: columns, two TSKgel-G3000H$_6$ columns (Tosoh Co., 5.0 cm i.d. × 60 cm); eluent, distilled THF; flow rate, 40 mL·min^{-1}; sample size, 0.63 g in 16 mL of THF. Chromatograms were detected with a refractometer (Shodex RI SE-62). Figure 1 shows a preparative SEC chromatogram; fractions B, D, and F, which correspond to OEG90, OEG54, and OEG18, respectively, were collected repeatedly with a fraction collector (Tosoh Model FC-8070 P&P) controlled by a personal computer. Fractions B and D were rechromatographed. Addition of isooctane to fraction D yielded a white precipitate (OEG54, 0.81 g), which was washed with *n*-hexane and dried under vacuum overnight. The yield of OEG54 based on the oligomeric mixture is 17%, which is much less than that expected from the chromatographic peak area of the OEG. Almost pure OEG90 was obtained from fraction B by the same procedure (0.09 g).

Mass Spectroscopy (MS). A double-focusing VG 70-250S mass spectrometer (VG Analytical Ltd.) was operated in the liquid secondary ion mass spectrometry (LSIMS) mode to obtain mass spectra of the OEG18 and OEG54 samples. The LSIMS gun was operated with a cesium ion beam (2 μA at 25 kV). The instrument was scanned from m/z = 300 to m/z = 2600, and the resolution was approximately 1000. The accelerating voltages are 8 kV for OEG18 and 6 kV for OEG54. The samples were dissolved in glycerol, which was used as a liquid matrix.

Differential Scanning Calorimetry (DSC). DSC measurements were performed by means of a Beckman differential scanning calorimeter (Model DSC7). Calibration of the temperature scale was carried out with standard materials, i.e., pure cyclohexane and indium. Carefully dried OEG54 samples (ca. 5 mg) were sealed into Al pans. These samples were heated to 80 °C and then rapidly cooled to 0 °C. From this temperature, the samples were heated through the melting region at several heating rates r in the range 1–20 K·min^{-1}. Melting temperatures at the respective heating rates were identified as temperatures corresponding to endothermic peaks. The heat of fusion of OEG54 was calculated by comparing the peak area of the endothermic peak with that of pure indium.

Light Scattering. Light scattering measurements were carried out with a commercial DLS-700 photometer (Otsuka Electronics Co., Ltd., Japan). Experimental details and measurement conditions were described in our previous paper.[5]

Spectral grade benzene (DOJINDO Lab. Co., Japan), which was used for calibration, was refluxed over calcium hydride and then distilled. Spectral grade methanol (DOJINDO Lab. Co., Japan) was used as the solvent: it was refluxed over Mg to remove water and then distilled. Solutions were prepared gravimetrically, and their polymer mass concentrations (c, in g·mL^{-1}) were calculated from their mass fractions w. In this calculation, we used Elias' data[13] for the solution density of PEG in methanol measured at 25 °C.

To calculate Rayleigh ratios of the solvent and sample solutions, we determined the Rayleigh ratio R_B of pure benzene at the temperature t = 25 °C by comparing the scattered intensity of pure benzene measured at 25 °C with those provided in the literature. In this study, we took Pike et al.'s R_B value as the literature value,[14] i.e., R_B = 11.84 × 10^{-6} cm^{-1} for t = 22 °C. On the basis of this value, we obtained R_B = 12.0 × 10^{-6} cm^{-1} as the R_B value at 25 °C from the ratio between the scattered intensity of benzene observed at 22 °C and that observed at 25 °C. For the values of the refractive indices $\tilde{n}$ at the wavelength of 633 nm and at 25 °C, we used 1.4938 for benzene[15] and 1.3274 for methanol.[16]

Specific refractive index increments $\partial\tilde{n}/\partial c$ of OEG18 and OEG54 in methanol at 25 °C were measured at λ_0 = 633 nm using a Brice KMX-16 differential refractometer (Chromatix Inc.). The measured values of $\partial\tilde{n}/\partial c$ are 0.140 and 0.141 mL·g^{-1} for OEG18 and OEG54, respectively.

Vapor Pressure Osmometry. VPO measurements were carried out using a Knauer type 11.00 osmometer. Solutions of OEG18 and OEG54 in benzene were measured at 45 °C. To calculate the number-average molecular weight, M_n, of OEG18 and OEG54, we used the commonly used calibration equation

$$\Delta R/c = K(1/M_n + A_2^{VPO}c + ...)$$

where ΔR is the bridge imbalance, c is the mass concentration, K is an instrumental constant, and A_2^{VPO} is the second virial coefficient. The value of K was determined by the measured value of $(\Delta R/c)_{c\to 0}$ of benzil (M = 210.2).

Carbon-13 NMR. Carbon-13 NMR spectra of OEG18 and OEG54 were recorded on a JEOL GSX400 spectrometer operating

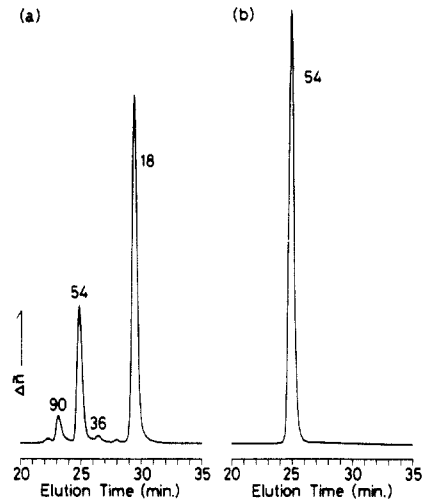

Figure 2. Analytical SEC chromatograms for (a) the oligomeric mixture and (b) pure OEG54. Separation conditions are the same for both chromatograms: columns, TSKgel-G2500H_8 × 2; flow rate, 1.0 mL·min^{-1}; eluent, THF; injection of samples, 2.05 mg·mL^{-1} × 300 μL.

at 100.40 MHz. The spectrometer was adjusted as follows: pulse mode, SGNNE (^{1}H noise decoupling without NOE); flip angle, 45°; pulse width, 4.0 μs; pulse repetition time, 11.2 s; spectrum width, 3000 Hz; line broadening (for exponential multiplication), 0.40 Hz; data points, 65536; digital resolution, 0.0005 ppm/point; number of scans, ca. 7000. The measuement temperature was 24.2 °C. The concentration (0.2 g) of the pure OEGs was resolved in 0.5 mL of deuterated chloroform. The chemical shifts are reported in ppm relative to TMS. The intensities of the signals were determined correctly by the integrated curves in the largely expanded spectra.

Proton NMR. ^{1}H NMR spectra were measured with a Bruker AC-200 spectrometer operating at 200 MHz. ^{1}H NMR data are reported in ppm relative to TMS. Measurement conditions were as follows: spin rate, 20 rpm; pulse width, 2.0 μs; sweep width, 1400 Hz; data points, 128K; number of scans, 64 or 32.

Previously dried OEG18 and OEG54 (ca. 0.16 g) were dissolved in deuterated dimethyl sulfoxide (DMSO-d_6, Aldrich 99.9 atom % D). The solutions were dried over type 3A molecular sieves in 1-mL volumetric tubes which were sealed by septum caps.[10] Sample solutions (ca. 0.5 mL) were injected into septum-capped NMR tubes (5 mm). Area determinations were carried out by integrations for three different separate spectra.

Results and Discussion

Our procedure for preparing pure OEGs is based on Booth et al.'s. procedure.[2] However, we have somewhat modified their procedure. First, sodium hydride (NaH) is used instead of sodium metal (Na) in preparing the sodium salts of the OEGs: using NaH, we can prepare the sodium salt more easily by the direct reaction between NaH and the terminal hydroxy groups of the OEGs. Analytical SEC chromatograms of the oligomeric glycol mixtures prepared by the direct reaction are similar to those of the mixtures prepared by Booth et al.'s procedure.[2]

Second, we have employed preparative high-performance SEC (HPSEC) to separate pure OEGs from the oligomeric mixtures: separation of the glycol mixtures is carried out faster with the HPSEC instrument than by classical gel filtration chromatography instruments such as used by Booth and co-workers. In our experiments, for example, about 20 g of the glycol mixture containing OEG18 can be separated in about 8 h using the HPSEC instrument.

The purity of the OEG54 sample was checked by analytical HPSEC. To gain high chromatographic resolution, we used four TSKgel-G2500H_{XL} columns. Figure 2 shows analytical SEC chromatograms for the glycol mixture and the pure OEG54 sample: no neighboring peak corresponding to OEG36 or OEG72 can be detected on either side of the chromatographic peak of OEG54. This observation indicates that the OEG54 sample is highly pure.

The purity of the OEG54 sample was also checked by DSC. It has been shown that the widths $\Delta T_{1/2}$ of the endothermic peaks of PEGs become larger as their polydispersity in molecular weight increases.[17] This is partially because the melting point of PEG varies with its molecular chain length. For example, the width of the endothermic peak of the OEG54 sample is about 3 times narrower than that of a commercial PEG-2000 at the heating rate r = 10 K·min^{-1}. Additionally, the width $\Delta T_{1/2}$ greatly depends on r: $\Delta T_{1/2}$ decreases with decreasing r.[17] For pure compounds such as pure indium, $\Delta T_{1/2}$ reduces to practically zero at the limit of $r \to 0$. Therefore, we measured $\Delta T_{1/2}$ at different r values and then estimated $\Delta T_{1/2}$ at r = 0. The extrapolated value of $\Delta T_{1/2}$ for the OEG54 sample is 0.2 K, indicating that its purity exceeds 98% mol.[17]

To determine the equilibrium melting temperature T_m of OEG54, we measured the endothermic peak T_{peak} at different heating rates (r = 1–20 K·min^{-1}) because the observed T_{peak} is greatly influenced by the heating rate: T_{peak} increases as the heating rate increases. In our experiments, T_{peak} observed at r = 20 K·min^{-1} is 2.7 K higher than those observed at $r \lesssim 2$ K·min^{-1}. However, T_{peak} observed at slow heating rates ($r \leq 2$ K·min^{-1}) is essentially constant. This observation was also reported by Stack et al.[18], who observed T_{peak} of an n-alkane, $C_{192}H_{386}$, to be almost constant in the range of $r \leq 1$ K·min^{-1}.

The melting temperature of OEG54 was determined as T_m extrapolated at zero heating rate (r = 0): a value T_m = 54.2 ± 0.2 °C was found. This value is consistent with the value T_m = 56 ± 1.43 °C expected from Wunderlich's equation[19] obtained for commercially available polydisperse PEGs and is in agreement with Yeates et al.'s findings:[2c] while T_m's of pure OEGs are appreciably higher than those of commercial PEGs for short chain lengths (x < 30), the difference between T_m of pure OEGs and those of the PEGs is essentially negligible for longer chain lengths (x > 30).

By extrapolation to the zero heating rate, we also calculated the heat of fusion ΔH at r = 0 for OEG54. The observed value of ΔH is 183 J·g^{-1}, which is smaller than that obtained by Yeates et al. for a pure sample of OEG45 (ΔH = 201 J·g^{-1}).[2c] However, our value is higher than that estimated from Buckley and Kovac's data[20] obtained for commercial PEG samples.

Mass Spectroscopy. In general, it is difficult to obtain molecular ions of high-molecular-weight oligomers because of their very low volatility. Moreover, polyglycol oligomers such as PEG yield no molecular ions by normal electron impact MS. For these oligomers, fragment ions are prominent particularly at low masses.[21] For pure OEG samples, it has been reported that MS measurements performed for OEG9 and OEG15 have only yielded spectra with a repeat pattern of fragments arising from successive loss of ethoxy units and no molecular ions can be observed.[2] However, recent developments in the ionization process enable us to observe relatively high-molecular-weight molecular ions. For example, field desorption (FD-MS)[22] and laser desorption (LD-MS)[23] mass spectroscopy were favorably employed to determine the molecular weight distributions of commercial PEGs.

Figure 3 shows a SIMS-MS spectrum of the pure OEG18 sample. A strong peak corresponding to its molecular ion

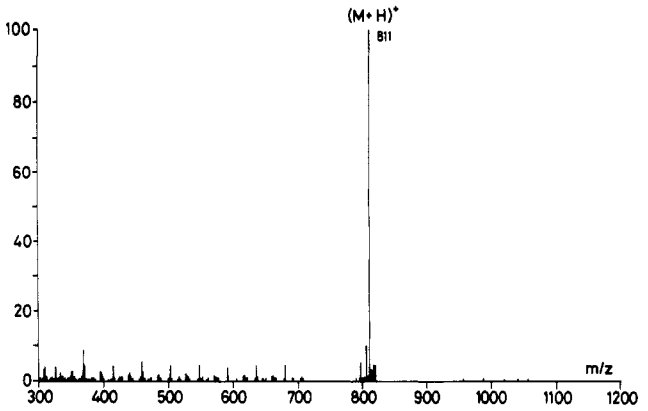

Figure 3. SIMS mass spectrum of the OEG18 sample.

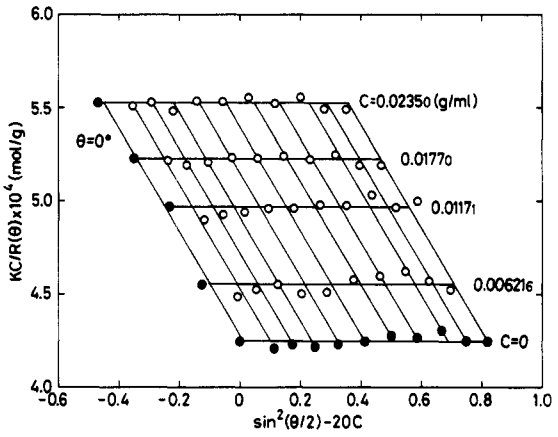

Figure 4. Zimm plot of the OEG54 sample in methanol at 25.0 °C.

$(M + H)^+$ (m/z = 811) is observed. This spectrum gives evidence that the sample consists of pure OEG18. Other weak peaks are considered to correspond to fragments (m/z = 679, 635, ...) arising from successive loss of ethoxy units (ΔM = 44). In the SIMS-MS spectrum of the OEG54 sample, we can observe a major peak (m/z = 2396) corresponding to its molecular ion $(M + H)^+$. Although other relatively strong peaks are observed in low-mass regions, the major peak indicates that the sample corresponds to pure OEG54.

Light Scattering. Figure 4 shows a Zimm plot for OEG54 in methanol at 25 °C: no angular dependence is observed. From the intercept at zero scattering angle (θ = 0°) and zero concentration (c = 0), we have obtained a value M_W = 2350 ± 30. The error in M_W is mainly due to the somewhat scattered data. In the calculation of M_W, we used the corrected Rayleigh ratio R_B mentioned in the Experimental Section, i.e., $R_B = 12.0 \times 10^{-6}$ cm^{-1}. For the OEG18 sample, its M_W value was determined from the intercept of its Zimm plot: the measured M_W is 800 ± 20. The observed M_W values of both OEG18 and OEG54 are in fairly good agreement with the molecular weights M = 810.9 for OEG18 and M = 2397 for OEG54 expected from their chemical formulas, respectively.

The good agreements described above not only show that our LS instrument is well adjusted but also indicate that these pure OEGs samples can be used as standards for determining absolute intensities of scattered light. Indeed, low-molecular-weight compounds have been used as standards for calibrating LS instruments.[11] Unfortunately, however, only a limited number of compounds have been examined in a few solvents because of their weak excess scattered light intensities. Nevertheless, it is still interesting to determine R_B with the use of the pure OEGs for the following reasons. First, for the wavelength λ = 633 nm, the literature values of R_B so far reported have been measured only with absolute LS photometers, which are not used in usual LS measurements for polymer solutions. Second, there are relatively large differences among the literature values of R_B:[15] for example, Pike's R_B value is about 6% smaller than Kaye et al.'s value $R_B = 12.63 \times 10^{-6}$ cm^{-1}. Contrary to this, the values of R_B for λ = 436 and 543 nm have been determined and confirmed rigorously by various methods and by many authors.[24]

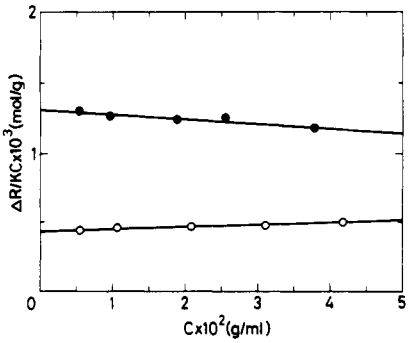

Figure 5. Vapor pressure osmometry results for the (●) OEG18 and (○) OEG54 samples measured in benzene at 45 °C. Bridge imbalance ΔR divided by calibration factor K times sample concentration c is plotted as a function of c.

Using the observed ratios between the measured M_W and true M expected for OEG18 and OEG54, we have obtained a value $R_B = 12.2 \times 10^{-6}$ cm^{-1} at 25 °C. This value is slightly larger than $R_B = 12.0 \times 10^{-6}$ cm^{-1} estimated from Pike's R_B value as described in the Experimental Section. On the other hand, our value is somewhat smaller (3.5%) than Kaye et al.'s R_B value mentioned above.[16]

As Figure 4 shows, we have obtained normal Zimm plots for OEG54 as well as for OEG18: no strong downturn at lower scattering angles is observed. This indicates that not only the sample solutions are purified optically but also no large aggregates exist in the solutions. We have already shown a similar angular dependence for OEG18 in acetonitrile.[5] These findings are in accord with Elias and Lys's[8] conclusion indicating no association occurs in methanolic solutions of low-molecular-weight PEGs ($M < 10^4$). However, contrary to this, Strazielle[25] showed a strong downturn at low angles in early times ($M > 10^4$). Moreover, Zhow and Brown[26] have recently shown similar strong downturns for PEOs in methanol ($M > 4 \times 10^4$) and suggested large aggregates in the solution. They have also suggested that the lower the molecular weight of PEG, the larger the size of the aggregate becomes. Although it is not clear why the difference in the scattering phenomena arises, one reason for the discrepancies in experimental conclusions may be due to the sources of the PEG and PEO samples used.[27] Similar problems have also been discussed for aqueous PEG solutions, and conflicting results have been reported.[28,29] In any event, the problem is complicated and here we do not discuss it further.

From the Zimm plots, the second virial coefficients A_2 of OEG18 and OEG54 in methanol have been obtained: $A_2 = 3.42 \times 10^{-3}$ for OEG18 and 2.83×10^{-3} mL·mol·g^{-2} for OEG54, respectively. These values are in good agreement with those observed by Elias and Lys.[8]

Vapor Pressure Osmometry. Figure 5 shows the concentration dependence of $\Delta R/Kc$ for OEG18 and OEG54 measured in benzene at 45 °C. As mentioned in the Experimental Section, a linear relation between $\Delta R/Kc$ and c is observed for both OEGs. However, while the slope of the straight line for OEG18 gives a negative value of $A_2^{VPO} = -3.21 \times 10^{-3}$ mL·mol·g^{-2}, that for OEG54 gives a positive $A_2^{VPO} = 1.42 \times 10^{-3}$ mL·mol·g^{-2}. This behavior is in accord with results reported earlier by other authors.[8,9]

Table I
Measured Molecular Weight Values for Pure OEG18 and OEG54

sample	M(formula)	M_w(LS)	M_n(VPO)	M_n(^{13}C)	M_n(^{1}H)
OEG18	810.9	800	763	863	801
OEG54	2396.7	2350	2290	2390	2300

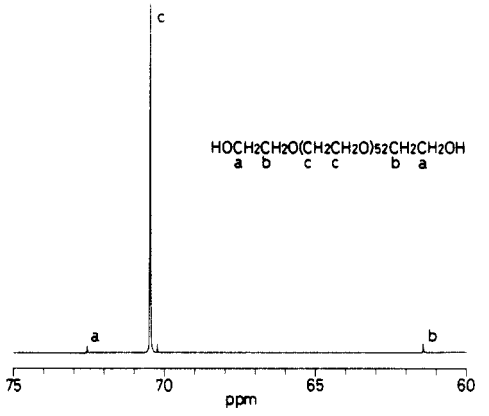

Figure 6. Quantitative 100-MHz ^{13}C NMR spectrum of the pure OEG54 sample measured in deuterated chloroform.

From the intercepts of the lines at $c = 0$, we have obtained M_n values of the OEGs: the values thus obtained are listed in Table I. They are in good agreement with the molecular weights M expected from their chemical structures. However, the differences between the M_n values and those M expected from their chemical formulas (about 6% for both OEGs) exceed experimental errors. These M_n values were determined on the basis of the assumption that the calibration factor K defined by the molecular weight of benzil is independent of the molecular weights of solutes. However, several authors[30,31] have shown that K often depends not only on the solvents used but also on the molecular weights of the oligomers. For instance, recently, Marx-Figini et al.[31] revealed that M_n determined by VPO is greater than the true M_n for commercial monodisperse polystyrenes in various solvents. In our previous study,[32] we also observed that K increases with increasing molecular weight of pure oligostyrenes in benzene: it was found that the value of K for $x = 20$ oligostyrene is about 20% larger than that for $x = 2$. Similarly, the differences in the M_n values of the OEGs can be ascribed in part to the molecular weight dependence of K.

Measurement conditions in VPO experiments may be the source of the discrepancies in M_n values. For example, Chylewsky and Simon[33] showed that drop size varies with sample concentration and heat capacities of thermistors. Furthermore, differences in the design of VPO instruments may often be the main sources of discrepancies in measured data: Stofer and Elias[34] showed that a Mechrolab instrument gives data different from those obtained with a Perkin-Elmer instrument.

Wrong extrapolation of $\Delta R/Kc$ to $c \rightarrow 0$ for associating solutions may be another reason for the deviation of measured M_n values from true ones. Elias and Lys[8] concluded that PEG molecules associate in benzene, acetonitrile, dioxane, and carbon tetrachloride. Additionally, Sato and Nakamura[9] indicated association of low-molecular-weight PEGs ($M < 2000$) in benzene. Thus the extrapolated values of $\Delta R/Kc$ to $c \rightarrow 0$ possibly give smaller M_n values than the true M_n.[35]

^{13}C NMR. Figure 6 shows a ^{13}C NMR spectrum measured for the OEG54 sample. For the OEG18 sample, a spectrum similar to this has also been observed. In these spectra, four separate peaks are observed: the largest signal corresponds to the backbone carbons (CH_2CH_2O; 70.5 and 70.2 ppm), and two other signals (61.4 and 72.5 ppm) correspond to the two terminal carbons. The spectrum gives evidence that the sample is not a cyclic compound like crown ethers but a linear chain molecule. In fact, each peak can be assigned by comparing the spectrum of the OEGs to those of similar compounds.

It is widely believed that ^{13}C NMR gives no quantitative information on the number of carbon atoms in compounds. However, we can obtain quantitative ^{13}C NMR spectra, if we can choose appropriate spectral parameters so as to ensure suppression of nuclear Overhauser effects (NOE) and a sufficient pulse delay time which is 5–10 times larger than the largest spin–lattice relaxation time (T_1).[36] As described in detail in the Experimental Section, the SGNNE mode is such a measurement mode that gives quantitative spectral data. Recently, Laude et al.[37] determined M_n values of two commercial PEG standard samples (PEG600 and PEG1450) from quantitative ^{13}C NMR spectra which were obtained with both the usual spinning methods and a special recycle flow method. It has been shown that M_n values can be determined not only more correctly but also in shorter times with a flow method than with the usual spinning method. Nevertheless, it is still interesting to determine M_n values of our pure OEG samples with the usual spinning methods because one usually uses commercially available NMR instruments.

For PEG, M_n values are calculated by the following equation:

$$M_n = \{(S/S_i) + 2\}M_0 + 18.0$$

where M_0 is the molecular weight of the repeating unit ($M_0 = 44.0$), S is the signal area of the backbone carbons, and S_i (i = a or b) is that of the signal a or b corresponding to the terminal carbons. Although the difference in signal areas between signals a and b cannot be seen in Figure 6, S_a is somewhat (about 2–3%) greater than S_b. In the present study, we choose i = b in the calculation of M_n merely because Laude et al.[37] calculated M_n values from the ratio between S and S_b. The M_n values thus determined are listed in Table I. Good agreements between measured M_n and true M are observed, especially for OEG54: the difference is less than 1%. These observations indicate that we can obtain average chain lengths of PEG molecules quantitatively from ^{13}C NMR spectral data.

^{1}H NMR. In spite of the simple chemical structure of PEGs, it is usually difficult to determine their M_n quantitatively by ^{1}H NMR not only because the signal of the terminal hydroxy protons is small but because both the position and strength of the signal vary with sample concentration, temperature, and impurities such as water. However, recently Dust et al.[10] revealed that the signal observed in DMSO-d_6 shows a clean triplet (at 4.56 ppm) well separated from that of backbone protons (3.0–4.0 ppm) and the peak position is independent of experimental conditions. In their study, they reported that observed M_n values agree well with those of manufacturers' values for commercial PEG standard samples.

Figure 7 shows a ^{1}H NMR spectrum for OEG54 in DMSO-d_6. As already reported by Dust et al.,[10] a clear triplet of the terminal hydroxy protons and a large central singlet of the backbone protons appear at 4.53–4.58 and 3.51 ppm, respectively. Also for OEG18, a similar spectrum was also obtained. In our spectra, practically no spinning sidebands are observed, indicating that the NMR instrument is well adjusted.

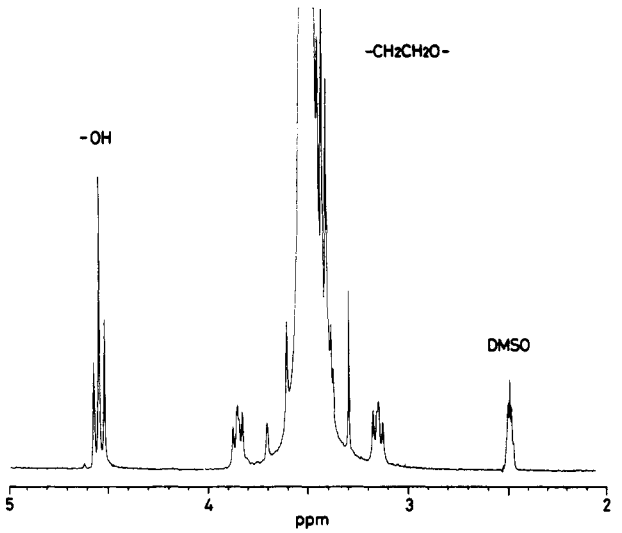

Figure 7. 200-MHz ^{1}H NMR spectrum of the pure OEG54 sample measured in DMSO-d_6.

We can determine M_n of the pure OEGs from these NMR spectra by the following equation:

$$M_n = (S_b/2S_{OH})M_0 + 18.0$$

where S_b and S_{OH} are the integrals of the backbone and hydroxy protons, respectively. Values of M_n thus determined for the OEG54 and OEG18 samples are listed in Table I. The observed values are in fairly good agreement with those expected from their chemical formulas, especially for OEG18.

In the determination of M_n values, appropriate instrumental parameters must be chosen carefully for both acquisition and processing of data because the ratio S_{OH}/S_b is significantly small for moderate molecular weight ($M > 1000$) PEGs: for OEG54, the ratio is about 0.01, which would be nearly equal to the practical error limits. Therefore, we have investigated the effects of the instrumental parameters on errors in the S_{OH}/S_b ratio. As a result, it has been found that the precision of the results depends mostly on the number of spectral data points in acquiring fid signals. For our OEG samples, the usual number of acquistition data points (16 kbit), which is routinely used for identifying low-molecular-weight compounds, have given values greater than the molecular weight values by more than 20%. On the other hand, a larger number of data points (128 kbit) enables us to obtain more correct molecular weight values. In particular, the observed M_n value of OEG18 is in fairly good agreement with the correct one as shown in Table I.

Conclusion

Two pure oligo(ethylene glycol)s, octadeca(ethylene glycol) (OEG18) and tetrapentadeca(ethylene glycol) (OEG54), have been prepared by stepwise synthesis followed by preparative SEC. Our OEG54 is a pure OEG and has the longest chain length reported hitherto: its molecular weight, M = 2396.7, is greater than Yeates et al.'s OEG45 by about 400.

Characterization of pure OEG54 and OEG18 samples has been performed by mass spectroscopy, light scattering, vapor pressure osmometry, ^{13}C NMR, and ^{1}H NMR. In general, the observed molecular weights of these pure OEG samples measured by these methods are in good agreement with those expected from their chemical formulas. This indicates that the OEG samples are undoubtedly what we expected. In particular, the fairly good agreement between observed and expected molecular weights in ^{1}H NMR in DMSO-d_6 show that ^{1}H NMR is a convenient and exact method for determining M_n values of PEG. Using well-adjusted ^{1}H NMR instruments, we can determine the M_n values in a short time (ca. 40 min) more easily and exactly than other characterization methods.

Finally, the pure OEGs can be used as model compounds in investigating physical and chemical properties of PEG. For example, it is of interest to investigate conformational properties of PEG chains in the oligomeric region, where chain dimensions greatly depend on the chain lengths of the oligomers.

Acknowledgment. We gratefully acknowledge Ms. T. Tozuka and Mr. S. Nakada for the SEC measurements and analysis and Dr. Y. Nagawa for the ^{13}C NMR measurements. We also thank Mr. T. Baba for his assistance in our use of his DSC apparatus and Dr. K. Hayamizu for her useful assistance and discussion on ^{1}H NMR measurements and data analysis.

References and Notes

(1) Bömer, B.; Heitz, W.; Kern, W. *J. Chromatogr.* **1970**, *53*, 51.
(2) (a) Marshall, A.; Mobbs, R. H.; Booth, C. *Eur. Polym. J.* **1980**, *16*, 881. (b) Teo, H. H.; Mobbs, R. H.; Booth, C. *Eur. Polym. J.* **1982**, *18*, 541. (c) Yeates, S. G.; Teo, H. H.; Mobbs, R. H.; Booth, C. *Makromol. Chem.* **1984**, *185*, 1559.
(3) Teo, H. H.; Marshall, A.; Booth, C. *Makromol. Chem.* **1982**, *183*, 2265.
(4) Craven, J. R.; Tyrer, H.; Li, S. P. L.; Booth, C.; Jackson, D. *J. Chromatogr.* **1987**, *387*, 233.
(5) Kinugasa, S.; Hattori, S. *Polym. J.* **1990**, *22*, 1059.
(6) Cambell, C.; Viras, K.; Masters, A. J.; Craven, J. R.; Hao, Z.; Yeates, S. G.; Booth, C. *J. Phys. Chem.* **1991**, *95*, 4647.
(7) Sicotte, Y.; Rinfret, M. *Trans. Faraday Soc.* **1962**, *58*, 1090.
(8) Elias, H.-G.; Lys, H. *Makromol. Chem.* **1966**, *92*, 1.
(9) Sato, H.; Nakamura, R. *Nippon Kagaku Zasshi* **1965**, *86*, 168.
(10) Dust, J. M.; Fang, Z.; Harris, J. M. *Macromolecules* **1990**, *23*, 3742.
(11) Utiyama, H. In *Light Scattering from Polymer Solutions*; Huglin, M. B., Ed.; Academic: London, 1972.
(12) Kinugasa, S.; Hattori, S. *J. Natl. Chem. Lab. Ind.* **1990**, *85*, 129.
(13) Elias, H.-G. *Makromol. Chem.* **1967**, *103*, 214.
(14) Pike, E. R.; Pomeroy, W. R. M.; Vaughan, J. M. *J. Chem. Phys.* **1975**, *62*, 3188.
(15) Huglin, M. B.; O'Donohue, S. J.; Radwan, M. A. *Eur. Polym. J.* **1989**, *25*, 543.
(16) Kaye, W.; McDaniel, J. B. *Appl. Opt.* **1974**, *13*, 1934.
(17) Marshall, A.; Domszy, R. C.; Teo, H. H.; Mobbs, R. H.; Booth, C. *Eur. Polym. J.* **1981**, *17*, 885.
(18) Stack, G. M.; Mandelkern, L.; Kröhnke, C.; Wegner, G. *Macromolecules* **1989**, *22*, 4351.
(19) Wunderlich, B. *Macromolecular Physics*; Academic: New York, 1980; Vol. 3.
(20) Buckley, C. P.; Kovacs, A. J. *Prog. Colloid Polym. Sci.* **1975**, *58*, 44.
(21) Lee, A. K.; Sedgwick, R. D. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 685.
(22) Lattimer, R. P.; Hansen, G. E. *Macromolecules* **1981**, *14*, 776.
(23) Cotter, R. J.; Honovich, J. P.; Olthoff, J. K.; Lattimer, R. P. *Macromollecules* **1986**, *19*, 2296.
(24) Kratohvil, J. P.; Deželić, Gj.; Kerker, M.; Matijević, E. *J. Polym. Sci.* **1962**, *57*, 59.
(25) Strazielle, P. C. *Makromol. Chem.* **1968**, *119*, 50.
(26) Zhou, P.; Brown, W. *Macromolecules* **1990**, *23*, 1131.
(27) Elias, H.-G. *Angew. Chem.* **1961**, *73*, 209.
(28) Polik, W. F.; Burchard, W. *Macromolecules* **1983**, *16*, 978.
(29) Devanad, K.; Selser, J. C. *Nature* **1990**, *343*, 739.
(30) (a) Brzeziński, J.; Glowala, H.; Kornas-Calka, A. *Eur. Polym. J.* **1973**, *9*, 1251. (b) Morris, C. E. M. *J. Polym. Sci., Polym. Symp.* **1976**, *55*, 11.
(31) Marx-Figini, M.; Figini, R. V. *Makromol. Chem.* **1980**, *181*, 2401.
(32) Hattori, S.; Nakahara, H.; Kamata, T. *Polymer 85 Prep. (Int. Symp. Characterization Anal. Polym.)* **1985**, 388.
(33) Chylewsky, C.; Simon, W. *Helv. Chim. Acta* **1964**, *47*, 515.
(34) Stofer, B. H.; Elias, H.-G. *Makromol. Chem.* **1972**, *157*, 245.
(35) Elias, H.-G. In *Light Scattering from Polymer Solutions*; Huglin, M. B., Ed.; Academic: London, 1972.
(36) Mooney, J. R. In *Analytical NMR*; Field, L. D., Sternhell, S., Eds.; John Wiley & Sons: Chichester, 1989.
(37) Laude, D. A.; Wilkins, C. L. *Macromolecules* **1986**, *19*, 2295.

Registry No. OEG54, 25322-68-3.