Synthesis and Characterization of Oligo(poly(ethylene glycol) fumarate) Macromer

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ABSTRACT: A novel oligomer based on alternating fumaric acid and poly(ethylene glycol) (PEG) units was synthesized and characterized. End group analysis by nuclear magnetic resonance (NMR) spectroscopy showed that the oligo (PEG fumarate) (OPF) had end PEG chains and multiple fumarate groups along its macromolecular chain. According to thermal characterization by differential scanning calorimetry (DSC), the crystallinity of OPF was found to be lower than PEG. The molecular weight and the degree of oligomerization of OPF determined by gel permeation chromatography (GPC) revealed that the conversion of OPF was substantially affected by the steric factors associated with large PEG chains. OPF was cross-linked using radical polymerization in the presence of either a chemical initiator or photoinitiator. As the OPF cross-linked, the unsaturated fumarate bonds disappeared and the PEG proton peak broadened in the NMR spectra. The cross-linked OPF gel showed swelling behavior that was dependent on the molecular weight of PEG. This novel cross-linkable PEG macromer is the first macromer with unsaturated double bonds along its macromolecular chain that allows for the preparation of hydrogels with tailored structure and properties.

Introduction

Poly(ethylene glycol) (PEG) based macromers have been extensively investigated for use in hydrogel preparation.[1−3] These PEG macromers, for example, have been prepared from block copolymers between PEG and biodegradable polyesters.[4−7] Typically, PEG macromers have been based on (meth)acrylation of PEG based polymers, where the (meth)acrylate group functions as the cross-linkable moiety. PEG di(meth)acrylate has been cross-linked by a variety of methods including photoirradiation.[8−11] The photocross-linking of PEG acrylates has been extensively explored as a means to coat PEG onto surfaces of polymeric materials and biological tissues.[6,8] The use of PEG mono(meth)acrylate has resulted in an interesting comb-shape polymer after polymerization.[12] A star PEG macromer, prepared by Peppas et al., has been cross-linked by UV light in the presence of PEG diacrylate, resulting in hydrogels with greater swelling than those formed with PEG diacrylate.[13] The cross-linking of these PEG acrylates has been systematically studied in terms of polymerization kinetics. Their resulting hydrogel properties have also been characterized with rubber elasticity theory.[9−11,14,15]

A new type of PEG macromer based on the photodimerization of cinnamylidene groups has also been synthesized.[16] This light-sensitive PEG macromer has been cross-linked by long wavelength (>300 nm) UV irradiation; however, the photo-cross-linked PEG hydrogels can undergo photoscission with UV irradiation at 254 nm. Various proteins such as myoglobin, hemoglobin, lactate dehydrogenase, and organophosphorus hydrolase have been immobilized into the photosensitive hydrogels, and their stability has been demonstrated. The mesh size and molecular weight between the cross-links of the cross-linked hydrogels have been investigated.[17,18]

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Fumaric acid, an unsaturated organic acid, has been used in the synthesis of a class of PEG macromers that, in contrast to those based on (meth)acrylate and cinnamylidene groups, can be radically polymerized in the presence or absence of comonomers. A number of poly(alkyl fumarate)s have been prepared by the radical polymerization of alkyl fumarate.[19−22] Fumarate bonds substituted with bulky alkyl groups have been easily polymerized since these bulky groups discourage bimolecular termination during polymerization. Biodegradable unsaturated polyesters based on fumaric acid have already been synthesized by polycondensation of fumaric acid with propylene glycol.[23−25] Similar biodegradable polymers have incorporated oligo(lactide) and oligocaprolactone with fumaric acid.[26] One of the polyesters, poly(propylene fumarate) (PPF), has been further transesterified with PEG to make poly(propylene fumarate-*co*-ethylene glycol) (P(PF-*co*-EG)), a biodegradable copolymer.[27,28] Macromers based on fumaric acid and biodegradable oligomers have been cross-linked in the presence of styrene, and the cross-linked macromers were degraded by hydrolysis.[26]

We have designed and synthesized a novel macromer based on PEG and fumaric acid. This novel PEG macromer is expected to have different properties from previous PEG macromers. The macromer may also be advantageous for biodegradation because of its multiple ester bonds in comparison with PEG (meth)acrylates. The macromer is further expected to be biocompatible because it consists of biocompatible components. Since the PEG macromer based on fumaric acid is composed of monomeric PEG fumarate of finite length, the physical properties of the macromer can be easily tailored by changing PEG molecular weight. In the preparation of the novel PEG macromer, we have also designed a simple one-pot reaction between PEG and fumaryl chloride that may be useful for other applications. The reaction is affected by factors such as PEG molecular weight and reactant molar ratio. The interpretation and

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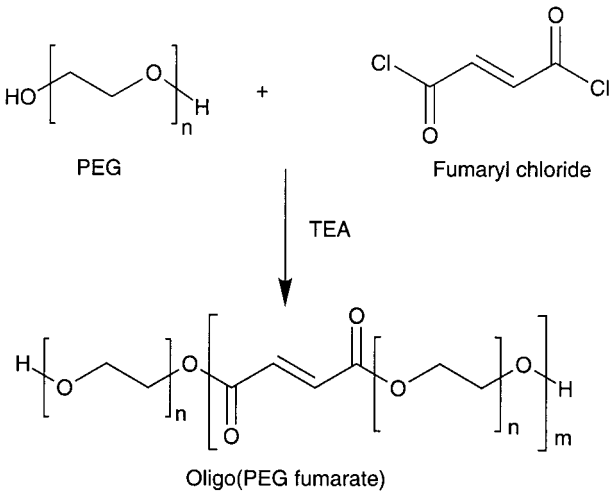
Scheme 1. Synthetic Reaction for the Preparation of OPF



modulation of those factors involved in the condensation reaction will provide useful information that is applicable to the preparation of various macromers with desirable properties as well as the resulting hydrogels.

Experimental Section

a. Materials. PEG (MW = 1000, 3350, and 4600) (PEG 1.0K, 3.4K, and 4.6K, respectively), trifluoroacetic anhydride (TFAA), calcium hydride, ammonium persulfate, and triethylamine were purchased from Aldrich (Milwaukee, WI). Fumaryl chloride was obtained from Acros (Pittsburgh, PA) and distilled before use. Anhydrous methylene chloride was obtained by distillation after the reflux for 2 h in the presence of calcium hydride. Ascorbic acid was obtained from Sigma (Saint Louis, MO) and bis(2,4,6-trimethylbenzyl)phenylphosphine oxide was given by Ciba Specialty Chemicals (Terrytown, NY). Other solvents were of reagent grade and were used without purification.

b. Methods. 1. Synthesis of Oligo(PEG fumarate) (OPF). OPF was prepared by the reaction represented in Scheme 1. Thirty grams (0.03 mol) of PEG 1.0K (50 g for PEG 3.4K and 4.6K) was dried by azeotropic distillation as follows. After dissolving PEG in 250 mL of toluene, 150 mL of toluene was distilled off, and the remaining toluene was further removed under reduced pressure. The dried PEG 1.0K was dissolved in 250 mL of anhydrous methylene chloride. Fumaryl chloride (0.3 mol) and triethylamine (0.3 mol) were simultaneously added to the PEG solution in an ice bath over 5 h while the reaction mixture was vigorously stirred. For the oligomerization of PEG 3.4K and 4.6K, 500 mL of anhydrous methylene chloride was used. To investigate the effect of the reactant ratio on the OPF molecular weight, three different molar ratios of PEG 1.0K to fumaryl chloride were used (1:0.8, 1:0.9, and 1:0.98). OPF from PEG of different molecular weights (OPF 1.0K, 3.4K, and 4.6K from PEG 1.0K, 3.4K, and 4.6K) was prepared by the same reaction for PEG 1.0K at 1:0.9 molar ratio of PEG to fumaryl chloride. After dropwise addition of fumaryl chloride and triethylamine into the PEG solution, the reaction was run overnight at room temperature. Upon completion of the reaction, the solvent was removed by rotovaporation, and the residue was dissolved in 500 mL (1000 mL for OPF from PEG 3.4K and 4.6K) of warm ethyl acetate. Then, triethylamine hydrochloride salt was removed by filtration. The OPF was recrystallized twice from ethyl acetate and dried at reduced pressure. The OPF was kept in a refrigerator to avoid cross-linking at room temperature.

2. Characterization of OPF. The PEG macromers were characterized by a 250 MHz ^{1}H NMR (Bruker AC 250) in $CDCl_3$. The end group of OPF was analyzed by NMR measurements after dissolving the OPF with 5.0% v/v trifluoroacetic anhydride in $CDCl_3$.[29,30] The number-average molecular weight of OPF was calculated from the NMR spectra.

The OPF was analyzed by differential scanning calorimetry (DSC). DSC was performed on a TA Instruments model 2920 (Newcastle, DE) with a mechanical cooling accessory. The samples were analyzed at a heating rate of 10 °C/min from 0 to 70 °C. Melting points and the heat of fusion, ΔH_m (cal/g), were obtained from the thermograms. The percent crystallinity of OPF, X, was determined from the following equation:

$$X = \frac{\Delta H_m}{\Delta H_m^*} \times 100 \quad (1)$$

Here, ΔH_m^* is the theoretical heat of fusion of 100% crystalline PEG (49 cal/g).[31]

The molecular weight of OPF was also calculated by gel permeation chromatography (GPC). A Phenogel guard column (50 × 7.8 mm, 5 μm, mixed bed, Phenomenex, Torrence, CA) and a Phenogel column (300 × 7.8 mm, 5 μm, mixed bed, Phenomenex) were used to elute the samples at 1 mL/min chloroform flow rate. After obtaining the calibration curve with PEG standards (Polyscience, Warrington, PA), number-average (M_n) and weight-average (M_w) molecular weights were calculated by running OPF samples. The degree of oligomerization, $\bar{X}_n$, and the conversion of OPF, p, were determined by the following equations:

$$\bar{X}_n = \frac{M_{n,OPF}}{M_{n,PFU}} \quad (2)$$

$$\bar{X}_n = \frac{1 + r}{1 + r - 2rp} \quad (3)$$

Here, $M_{n,OPF}$, $M_{n,PFU}$, and r represent the M_n of OPF determined by GPC, the molecular weight of monomeric PEG fumarate, and [fumaryl chloride]/[PEG], respectively.

The OPF was characterized by FT-IR spectroscopy. Samples were prepared as KBr pellets, and the spectra were obtained on a Nicolet 500 spectrometer (Madison, WI).

3. Cross-Linking of OPF and Characterization of the Photo-Cross-Linked OPF Hydrogels. The OPF was cross-linked by radical polymerization. The cross-linking of the OPF was qualitatively analyzed by NMR measurements. To observe the cross-linking of OPF by photoirradiation, 0.2 g of OPF 3.4K and 0.002 g of bis(2,4,6-trimethylbenzyl)phenylphosphine oxide were dissolved in 1.0 mL of CD_3OD:DMSO-d_6 (1:1). The NMR spectrum of the OPF solution was recorded before and after 30 min photoirradiation in an Ultralum (Paramount, CA) ultraviolet light box. The cross-linking of OPF by the chemical initiators was investigated after dissolving 0.2 g of the OPF and 5.0 μg of ammonium persulfate and ascorbic acid in 1 mL of D_2O. The NMR spectrum of the OPF solution was recorded at 10 min, 1.5 h, 3.0 h, and 24 h after the addition of initiators.

The swelling of the cross-linked OPF was investigated by a gravimetric method. Samples for the swelling study were prepared by photoirradiation which was faster than chemical cross-linking. The solution for cross-linking was prepared by dissolving 1 g of OPF in 5 mL of 60% v/v dimethylformamide (DMF) in water. To investigate the effect of the amount of photoinitiator, 0.1, 0.15, and 0.2 mL of 10% (w/v) bis(2,4,6-trimethylbenzoyl)phenylphophine oxide in DMF were mixed with the OPF solution. The OPF solution was transferred to a polystyrene cell culture dish (60 × 15 mm, Fisher Scientific, Pittsburgh, PA) lined with Teflon film. The OPF solution was cross-linked by 1 h irradiation with UV light. The cross-linked OPF gels were cut into 12 mm diameter disks. The disks were dried at 0.25 Torr overnight and then weighed, W_i. The dry films were swollen in 20 mL of deionized distilled water (DDW) until an equilibrium was reached and then weighed again, W_s. The swollen gels were dried overnight at reduced pressure and weighed, W_d. The swelling ratio and the fraction of unreacted

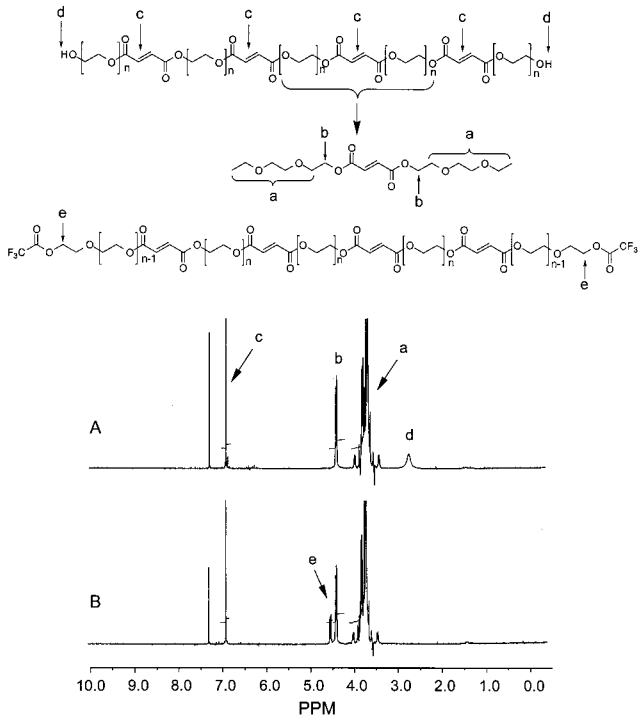


Figure 1. ^{1}H NMR spectra of an OPF 1.0K in the absence (A) and presence (B) of trifluoroacetic anhydride. The OPF 1.0K was prepared by the reaction between PEG 1.0K and fumaryl chloride at a 1:0.90 molar ratio. NMR measurements were carried out in $CDCl_3$ at room temperature.

macromer, sol fraction, were determined by the following equations:

$$\text{swelling ratio} = \frac{W_s - W_d}{W_d} \tag{4}$$

$$\text{sol fraction} = \frac{W_i - W_d}{W_i} \tag{5}$$

Here, swelling ratio represents the amount (grams) of water that can be drawn by 1 g of dry OPF gel rather than simple weight ratio between swollen and dry OPF gels.

Results and Discussion

Synthesis and Characterization of OPF. A novel macromer based on PEG and fumaric acid has been designed and prepared by a simple one-pot reaction. The reaction between PEG and fumaryl chloride resulted in the formation of PEG fumarate oligomers. The end group of the OPF was analyzed by using trifluoroacetic anhydride, a compound that immediately reacts with free hydroxyl groups to form trifluoroacetate.[29,30] The formation of trifluoroacetate shifted the attached methylene proton downfield, thus separating it from the other methylene proton peaks of PEG (Figure 1). Since trifluoroacetic anhydride cannot react with fumaric acid, this change in the NMR spectrum indicated the presence of end hydroxyl groups and therefore the termination of OPF by PEG. These end PEG chains may be useful for the immobilization of proteins and peptides due to their end hydroxyl groups.[32,33] These macromers may also be utilized to produce hydrogels with specific functions, such as molecular recognition and drug delivery. The previously described reaction can be used to prepare biodegradable macromers based on fumaric acid by reacting biodegradable polymers with end functional groups such as end-hydroxylated polycaprolactone and end-hydroxylated poly(α-hydroxy acid)s in the presence of fumaryl chloride.

The number-average molecular weight (M_n) of OPF was determined by NMR measurements with the assumption that the OPF had PEG end groups. The determined molecular weights of OPF are presented in Table 1. The OPF molecular weight was close to that determined by GPC calibrated with PEG standards.

The properties of OPF were dependent on the PEG molecular weight and the ratio between PEG and fumaryl chloride. As the PEG molecular weight increased from 1000 to 4600, the $\bar{X}_n$ determined by eq 2 decreased from 5.1 to 2.5. As the ratio of fumaryl chloride to PEG, r, decreased from 0.98 to 0.80, $\bar{X}_n$ also decreased from 5.67 to 3.6 and the M_n of OPF decreased from 7790 to 4990. The conversion of PEG and fumaryl chloride into OPF (p), as determined by eq 3, decreased as the PEG molecular weight increased. Specifically, as the PEG molecular weight increased from 1000 to 4600, p fell from 0.83 to 0.62 ($r = 0.9$) (Figure 2). However, a change in r did not cause a significant change in p. The calculated p values for OPF 1.0 K at $r = 0.98$, 0.90, and 0.80 were 0.83, 0.85, and 0.81, respectively. These effects of PEG molecular weight on oligomerization extent can be explained in terms of steric hindrance. As PEG molecular weight increases, the reactivity of end hydroxyl groups decreases since the larger PEG random coil exerts more steric hindrance. For example, the GPC chromatograms in Figure 3 indicate that the OPF 1.0K does not include any noticeable free PEG while OPF 3.4K and 4.6K do contain a small amount of free PEG. The results also show that the hydroxyl groups of low molecular weight PEG are more accessible to fumaryl chloride during the oligomerization. Figure 4 shows that the OPF molecular weight can be modulated by a change in r. According to the calculated $\bar{X}_n$ at various p

Table 1. Characterization Data of Various OPF Prepared From PEG of Different Molecular Weights and Fumaryl Chloride[a]

					GPC			NMR
sample	r	T_m (°C)	ΔH_m (cal/g)	% crystallinity	M_n	M_w	$\bar{X}_n$	M_n
PEG 1.0K		40.51 ± 1.65	28.9 ± 2.8	59.0	1260	1330		
PEG 3.4K		60.59 ± 1.00	40.1 ± 0.2	81.8	3960	4180		
PEG 4.6K		61.06 ± 0.78	44.2 ± 4.4	90.2	5080	5440		
OPF 1.0K	0.98	39.42 ± 1.18	21.2 ± 2.4	43.3	7790	16070	5.67	6720
OPF 1.0K	0.90	39.83 ± 0.27	25.9 ± 0.5	52.9	7000	11210	5.09	6840
OPF 1.0K	0.80	40.29 ± 1.01	27.0 ± 1.4	55.1	4990	6960	3.63	4630
OPF 3.4K	0.90	55.47 ± 0.52	35.1 ± 2.4	71.6	11610	22060	2.85	12400
OPF 4.6K	0.90	56.69 ± 0.01	35.9 ± 3.0	73.3	12600	22470	2.43	12260

[a] r is the molar ratio between fumaryl chloride and PEG. The melting temperature (T_m) and the heat of fusion (ΔH_m) were measured by DSC. Number-average (M_n) and weight-average (M_w) molecular weights were calculated by GPC and end group analysis using NMR. The degree of oligomerization, $\bar{X}_n$, was determined by eq 3. For DSC measurements, $n = 3$.

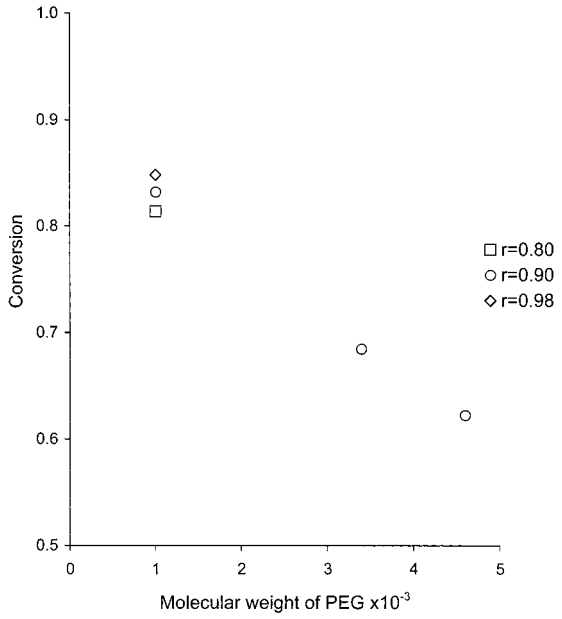


Figure 2. Conversion of OPF prepared from PEG 1.0K (for r = 0.80, 0.90, 0.98), 3.4K, and 4.6K.

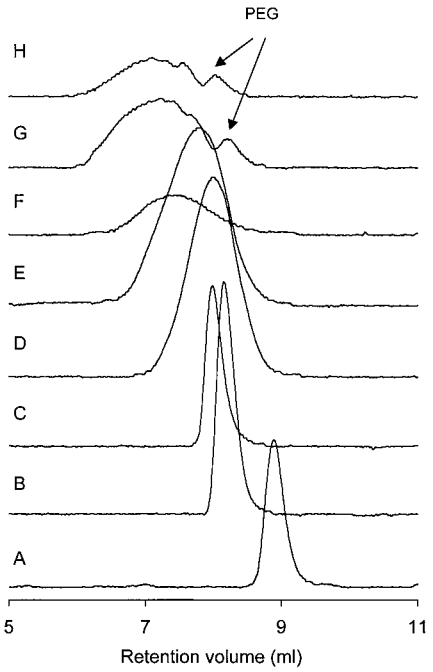


Figure 3. GPC chromatograms of PEG and OPF. PEG 1.0K (A), 3.4K (B), and 4.6K (C) were used for the preparation of OPF 1.0K at 1:0.80 (D), 1:0.90 (E), and 1:0.98 (F) molar ratio between PEG and fumaryl chloride, OPF 3.4K (G), and OPF 4.6K (H) at 1:0.90 molar ratio between PEG and fumaryl chloride.

values, the effect of r on $\bar{X}_n$ substantially increases as p is closer to 1.00. In reality, the polycondensation between fumaryl chloride and PEG cannot produce oligomers of high molecular weight mainly because of the steric factor of PEG. According to Figure 4, the highest achievable $\bar{X}_n$ in our experimental system was 6.0, 3.2, and 2.7 for PEG 1.0K, 3.4K, and 4.6K, respectively. However, the conversion of OPF may be improved by increasing the reaction time.

Thermal characterization of OPF by DSC showed that the OPF has a lower heat of fusion than PEG. A change in r also affected the heat of fusion of the OPF and thus the crystallinity. As r for OPF 1.0 K increases from 0.80

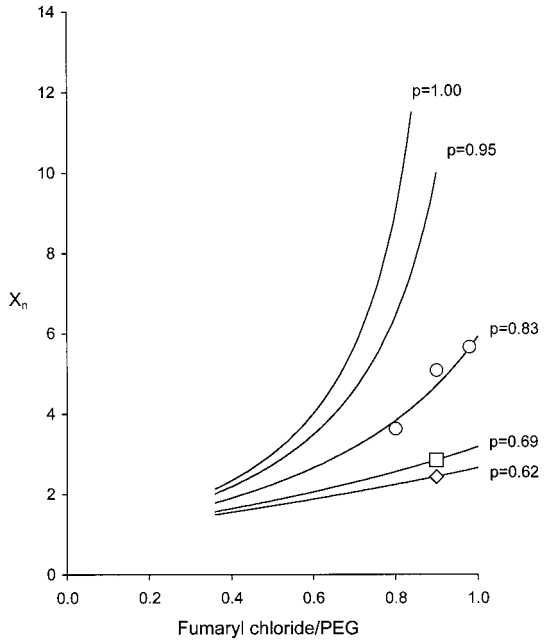


Figure 4. Dependence of the degree of oligomerization, $\bar{X}_n$, on the conversion, p, and monomer molar ratio, r. The degree of oligomerization at various conversions was calculated by using eq 3, and experimental data were fitted to the curves. For OPF 1.0K, OPF 3.4K, and OPF 4.6K, the determined p values, 0.83, 0.69, and 0.62, respectively, were used.

to 0.98, the heat of fusion decreases from 27.0 to 21.2 cal/g. These values are noticeably lower than 28.9 J/g, the heat of fusion of PEG 1.0K determined by DSC. Additionally, the melting temperature of OPF was lower than that of PEG. OPF 3.4K and 4.6K especially showed significant lower melting temperatures than PEG 3.4K and 4.6K while the OPF 1.0K had similar melting temperature to the PEG 1.0K. The melting temperatures of PEG 3.4K and 4.6K were 60.59 and 61.06 °C, while those of OPF 3.4K and 4.6K (r = 0.9) were 55.47 and 56.69 °C, respectively. The changes in the heat of fusion and melting temperature could be a result of conformational changes in the polymer backbones caused by oligomerization. The incorporation of rigid fumarate bonds could prevent close packing of the flexible PEG chains and thus cause a decrease in crystallinity as seen in Table 1. This decrease in crystallinity may result in the observed changes in melting temperature and heat of fusion in comparison with PEG.

The FT-IR spectra of OPF in Figure 5 also indicated successful incorporation of fumarate bonds into the macromer. In comparison with the IR spectra of PEG 1.0K and 3.4K, the IR spectra of corresponding OPF 1.0K and 3.4K showed a characteristic ester carbonyl stretch band at 1725 cm^{-1} in addition to an asymmetrical C−O−C stretching band at 1110 cm^{-1} and C−H stretch bands at 2890 cm^{-1}.

Characterization of the Cross-Linking of OPF by NMR. The OPF was cross-linked by radical polymerization. The cross-linking of OPF was initiated either by photoirradiation of bis(2,4,6-trimethylbenzyl)phenylphosphine oxide or by chemical initiation in the presence of ammonium persulfate and ascorbic acid. The cross-linking of OPF was qualitatively investigated by NMR spectroscopy, a useful method for the characterization of cross-linked gels.[34] Figure 6 shows the changes in the NMR spectrum of OPF 3.4K after cross-linking. Photoirradiation for 30 min cross-linked the OPF and

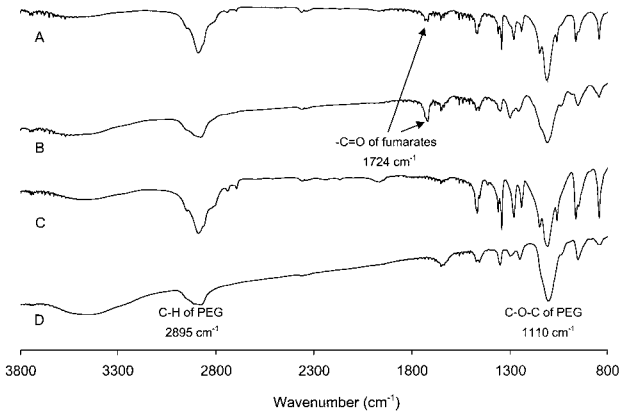


Figure 5. FT-IR spectra of OPF 3.4K (A) and OPF 1.0K (B) prepared from PEG 3.4K (C) and 1.0K (D).

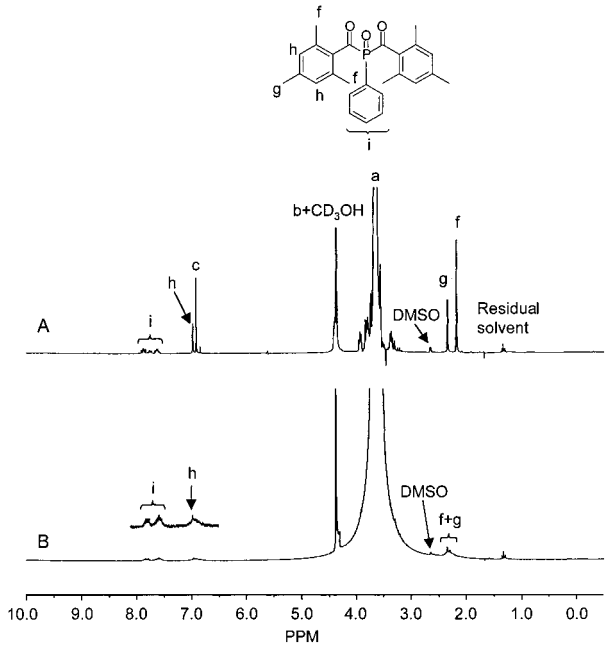


Figure 6. ^{1}H NMR spectra of OPF 3.4K before (A) and after (B) UV irradiation for 30 min in the presence of 1.0% w/w of bis(2,4,6-trimethylbenzyl)phenylphosphine oxide. NMR was measured in CD_3OD:DMSO-d_6 (1:1). The peak assignment of OPF was based on the chemical structures and notions in Figure 1.

caused the NMR band of unsaturated fumarate protons at 6.8 ppm to disappear and the PEG proton peak to dramatically broaden. The fumarate protons were consumed in the cross-linking reaction. The peak broadening may be related to decreased polymer mobility and thus a shorter relaxation time.[35,36]

In addition to photoirradiation of the OPF, radical polymerization using ammonium persulfate and ascorbic acid also cross-linked the OPF 3.4K. The chemical initiators required a longer time for the cross-linking of OPF than that needed with photoirradiation. Ten minutes after the addition of initiators, there was no significant change in the NMR spectrum of the OPF 3.4K (Figure 7A). After further time, the intensity of the fumarate proton peak noticeably decreased and the PEG proton peak broadened (Figure 7B−D). The OPF 3.4K started to form a gel at 3 h. The complete cross-linking of the OPF 3.4K caused the fumarate proton peak, b, to disappear in the NMR spectrum and the PEG proton peaks to broaden further as shown in Figure 7D.

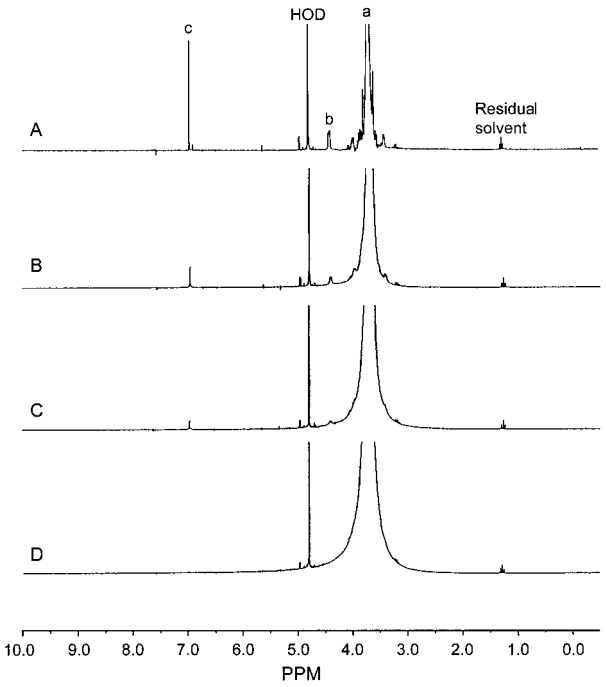


Figure 7. ^{1}H NMR spectra of OPF 3.4K at 10 min (A), 1.5 h (B), 3.0 h (C), and 24 h (D) after the addition of ammonium persulfate and ascorbic acid. NMR was measured in D_2O. The peak assignment of OPF was based on the chemical structures and notions in Figure 1.

Table 2. Swelling Properties of the Cross-Linked OPF Hydrogels[a]

sample	*r*	initiator (% w/w)	swelling ratio	sol fraction (%)
OPF 1.0K	0.90	1.0	5.67 ± 0.10	8.61 ± 0.24
OPF 1.0K	0.90	1.5	6.62 ± 0.04	10.48 ± 0.12
OPF 1.0K	0.90	2.0	5.91 ± 0.04	6.10 ± 0.11
OPF 3.4K	0.90	1.0	11.55 ± 0.61	11.65 ± 3.80
OPF 3.4K	0.90	1.5	12.61 ± 0.07	12.18 ± 0.16
OPF 3.4K	0.90	2.0	13.22 ± 0.10	12.15 ± 0.10
OPF 4.6K	0.90	1.0	16.01 ± 0.16	19.79 ± 0.10
OPF 4.6K	0.90	1.5	18.44 ± 0.21	20.06 ± 0.68
OPF 4.6K	0.90	2.0	19.91 ± 0.21	21.10 ± 0.41
OPF 1.0K	0.98	1.5	5.35 ± 0.07	5.87 ± 0.06
OPF 1.0K	0.80	1.5	11.03 ± 0.40	53.51 ± 1.00

[a] *r* is the molar ratio between fumaryl chloride and PEG. For all samples, $n = 3$.

Fumarates with bulky alkyl groups such as isopropyl *tert*-butyl fumarate, di-*tert*-butyl fumarate, and ditrimethylsilyl fumarate have been reported to form high molecular weight homopolymers by radical polymerizations.[19] Large alkyl groups have been known to reduce bimolecular termination, increase the polymerization rate, and increase the molecular weight of the resulting polymer. Considering the effect of the bulky alkyl groups on the polymerization of dialkyl fumarates, the presumed random coils of PEG in 60% (v/v) DMF in water might play a similar role as the bulky groups that help the OPF cross-link. The cross-linked OPF may be especially valuable for the surface coating of polymeric materials by photoirradiation.

Characterization of Swelling of the Cross-Linked OPF. The cross-linked OPF exhibited swelling characteristics of a hydrogel, with swelling ratios dependent on the molecular weight of PEG. Table 2 summarizes the results of the swelling studies. As the PEG molecular weight increased from 1000 to 4600, the swelling ratio of the cross-linked OPF by photoirradiation in the presence of 1.0% w/w initiator increased from 5.7 to

16.0. However, the concentration of the initiator did not significantly affect the swelling of the cross-linked OPF in the range from 1.0% to 2.0% (w/w). The increase in the swelling ratio with the increase in the PEG molecular weight may be due to the longer mesh size between cross-linkable fumarate bonds. As seen in Table 2, the sol fraction of the cross-linked OPF also increased with the increase in PEG molecular weight. The sol fraction of cross-linked OPF at 1.0% (w/w) of initiator increased from 8.6% to19.8% as the PEG molecular weight increased from 1000 to 4600.

The molar ratio of fumaryl chloride to PEG also affected the swelling of cross-linked OPF. As *r* increased from 0.80 to 0.98, the swelling ratio of the cross-linked OPF 1.0K in the presence of 1.5% w/w of photoinitiator decreased from 11.0 to 5.4. The change in swelling ratio of the cross-linked OPF 1.0K with the change in the reactant molar ratio may be associated with the change in sol fraction. The sol fraction of the cross-linked OPF 1.0K slightly increased from 6% to 10% as the reactant molar ratio decreased from 0.98 to 0.90, respectively. Further decrease in *r* from 0.90 to 0.80, however, dramatically increased the sol fraction from 10% to 54%, respectively, while the swelling ratio increased from 6.6 to 11.0. The effect of the molar ratio on the sol fraction might result from the change in the molecular weight of the OPF 1.0K. As *r* increased from 0.80 to 0.98, the determined molecular weight by GPC increased from 4990 to 7790. The increase in molecular weight caused an increase in viscosity of the OPF 1.0K solution. This increase in viscosity might affect the cross-linking by limiting the diffusion of radicals. As the viscosity increases, the limited diffusion of radicals may interfere with the termination of polymerization by bimolecular coupling.

The copolymerization of OPF with other monomers may also be useful for the preparation of polymeric gels with different physical properties. The cross-linked OPF may have different swelling properties from hydrogels of PEG acrylates or P(PF-*co*-EG) since the fumarate bonds of OPF are separated by finite PEG blocks. The OPF, therefore, may be more suitable for preparing hydrogels with a defined structure. Furthermore, the presence of multiple ester bonds as well as hydrophilic PEG backbones can facilitate the degradation of OPF in an aqueous environment. Vinyl monomers such as *N*-vinyl-2-pyrrolidinone and styrene have been especially effective as comonomers with fumarates.[23,25,26] The estimated *Q* and *e* values and monomer reactivity (r_1 and r_2) between diethyl fumarate and vinyl monomers also indicate that the pairs are favorable for forming copolymers.[20,21] Finally, the OPF may be advantageous for use as a cross-linking agent by improving the dispersion of polymeric resins because it is soluble in aqueous and organic solvents.

Conclusions

A novel macromer based on PEG and fumaric acid was successfully prepared by a simple reaction between PEG of different molecular weights and fumaryl chloride. The macromer was designed to contain end PEG chains and multiple fumarate bonds. The PEG molecular weight and the molar ratio of PEG and fumaryl chloride affected the molecular weight of OPF and its physical properties. The prepared OPF was cross-linked by radical polymerization initiated by photoirradiation and chemical initiation. The cross-linked OPF gels exhibited typical properties of hydrogels, which were dependent on the molecular weight of PEG and the reactant ratio between fumaryl chloride and PEG.

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