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Preparation of Poly(methacrylic acid-*g*-ethylene oxide) Microspheres

Introduction. Poly(methacrylic acid-*g*-ethylene oxide) (P(MAA-*g*-EO)) is a copolymer that has been shown to exhibit unique properties due to its ability to form reversible hydrogen-bonded complexes.[1,2] This complexation results in changes in the swelling characteristics upon a change of pH or temperature of the surrounding environment. At acidic pH values, the ethylene oxide chains associate with the poly(methacrylic acid) backbone of the copolymer to form a highly compact network. Upon raising the pH to alkaline values, this complexation reverses and the network swells.[1] This behavior presents a potential for use of such polymers in biosensors or as carriers for controlled drug delivery systems.[3]

P(MAA-*g*-EO) has been synthesized by means of a free-radical bulk polymerization.[1,2] However, for use in the physiological environment, this copolymer would be more feasible in the form of microspheres.

Experimental Section. A suspension polymerization technique was used to prepare microspheres of P(MAA-*g*-EO). A 500-mL three-neck flask, equipped with a reflux condenser, was employed for the suspension polymerization reaction. The suspending phase consisting of 300 mL of silicone oil (Dow 200 fluid, dielectric grade) was added to the flask and agitated at a rate of 250 rpm until its temperature reached 70 °C. The polymerizing phase solution consisted of 5 g of methacrylic acid (MAA; Aldrich Chemical Co., Milwaukee, WI) and 5 g of methoxypoly(ethylene glycol) monomethacrylate 1000 (M(1000)G; Polysciences, Warrington, PA) mixed with 2 wt % tetraethylene glycol dimethacrylate (TEGDMA; Polysciences) as a cross-linking agent, 0.2 wt % 2,2-azobis(2-methylpropionitrile) (AIBN, Aldrich) as an initiator, and 1 wt % poly(dimethylsiloxane-*b*-ethylene oxide) (P(DMS-*b*-EO) with 25% DMS; Scientific Polymer Products, Ontario, NY) as a surfactant. This mixture was added to the silicone oil, agitated at 400 rpm, and allowed to react for 3 h at 70 °C and for 2 h at 90 °C.

When the reaction was completed, the contents of the flask were poured into a 1000-mL beaker and allowed to cool for 30 min. Most of the silicone oil was decanted, approximately 1000 mL of deionized water was then added to the beaker, and the contents were stirred overnight. Subsequently, the particles were allowed to settle, and the water and remaining silicone oil were decanted. This washing procedure was repeated until no silicone oil remained.

The particle size distribution was determined by means of a Coulter Counter (Model ZM, Coulter Electronics, Luton, Bedsford, U.K.). In addition, the chemical composition of a sampling of dried particles was determined by means of a Fourier transform infrared (FTIR) spectrometer (Perkin-Elmer Model 1600, Norwalk, CT).

The equilibrium degree of swelling of the polymer microparticles was determined in buffer solutions of pH 4.75 and 7.4. Particles were isolated on microscope slides and allowed to dry for 24 h at room temperature and then for 24 h under vacuum. Their diameters were measured by examination under a microscope. The particles were then swollen in the buffer solution at 37 °C for 1 h. The particles were again examined under the microscope, and the final diameters were measured.

Results and Discussion. Developing the suspension polymerization technique involved variations in the suspending phase, the reaction temperature, the surfactant concentrations, and the agitation rate. Initially, a salting-out technique[4] was used by adding the water-soluble monomers, MAA and M(1000)G, to a saturated (26 wt %) sodium chloride solution. This two-phase mixture was agitated and allowed to react for 18 h at 60 °C. These reaction conditions were chosen because the bulk polymerization of P(MAA-*g*-EO) had successfully been completed at these conditions. The result of the suspension polymerization, however, was not the formation of microparticles but of a mass of gel.

In an attempt to understand this result, the same suspension polymerization technique was used to produce homopolymer microparticles of MAA or M(1000)G. Under these reaction conditions, M(1000)G polymerized to form microparticles; however, MAA did not polymerize. PMAA microparticles could, however, be produced if the reaction was run at 70 °C for 3 h and 90 °C for 2 h.

These reaction conditions could not be used for the polymerization of the copolymer in the presence of water, because water-swollen P(MAA-*g*-EO) underwent irreversible swelling at temperatures exceeding 70 °C, possibly due to PEG hydrolysis. Thus, the suspending phase was changed to an organic phase, and silicone oil was chosen because of its relative nontoxicity.

Suspension polymerization of P(MAA-*g*-EO) in silicone oil at the higher temperatures resulted in copolymer microspheres; however, the particles were highly agglomerated as shown in Figure 1. Performing the reaction in the presence of 1 wt % surfactant P(DMS-*b*-EO) significantly reduced this agglomeration as indicated in Figure 2.

The final adjustment made to the polymerization technique was the variation of agitation rate. Increasing the agitation rate from 250 to 400 rpm resulted in a significant

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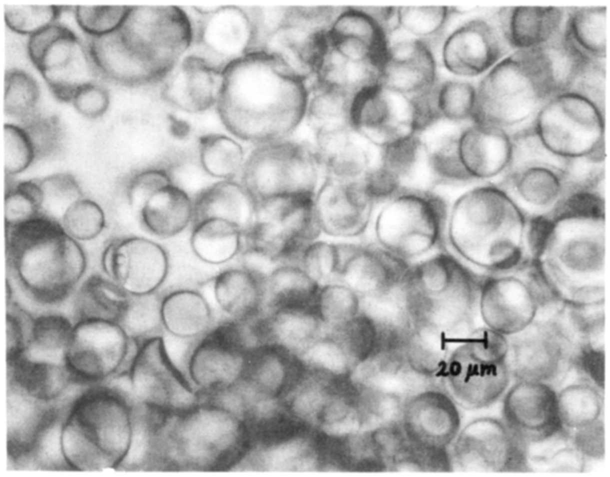

Figure 1. Agglomerated P(MAA-*g*-EO) microspheres swollen in water at 25 °C (10×).

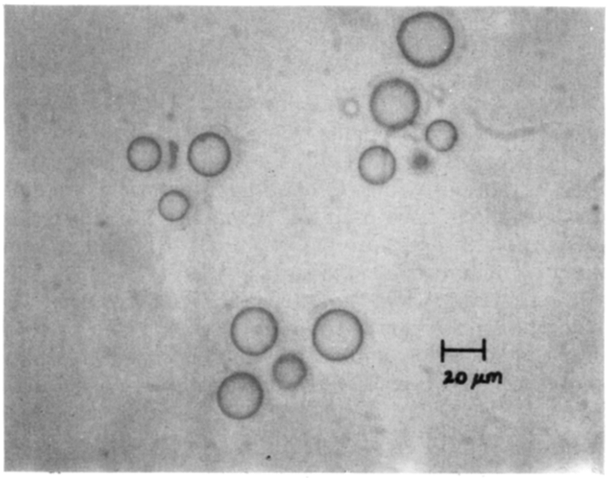

Figure 2. P(MAA-*g*-EO) microspheres prepared in the presence of P(DMS-*b*-EO) and swollen in water at 25 °C (10×).

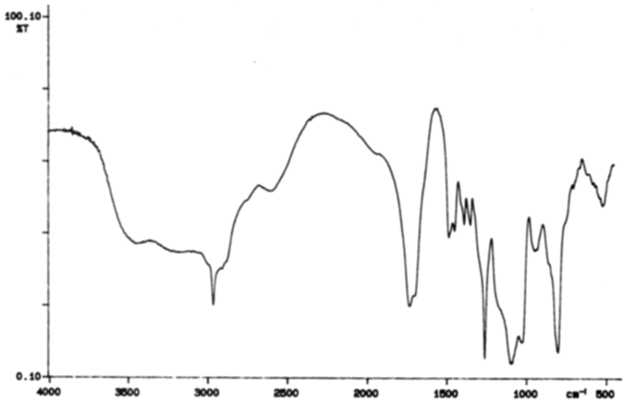

Figure 3. FTIR spectrum for P(MAA-*g*-EO) microspheres prepared without surfactant.

reduction in particle size. When the agitation rate was raised to 500 rpm, however, either the particles were too small to isolate or polymerization did not occur.

The FTIR spectrum for the P(MAA-*g*-EO) microspheres (Figure 3) indicates the presence of both methacrylic acid and poly(ethylene oxide) in the microspheres. Since accurate quantification by FTIR analysis is not possible, the copolymer composition was determined from the initial monomer content. Comparison of the FTIR spectrum of the particles prepared with and without surfactant indicated that surfactant was not incorporated into the copolymer network.

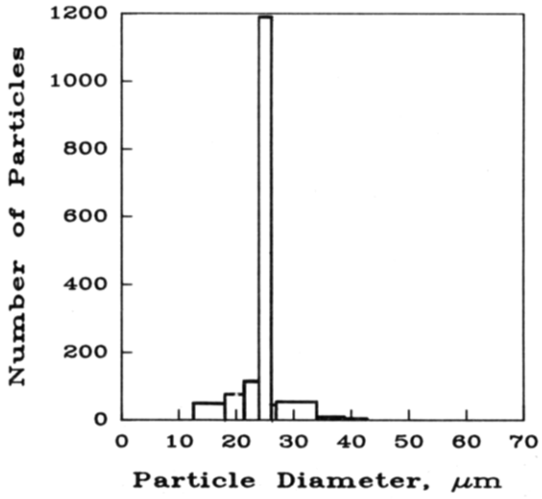

Figure 4. Particle size distribution for P(MAA-*g*-EO) microspheres prepared in the presence of 1.5 wt % P(DMS-*b*-EO) as a surfactant. The particles were swollen in an electrolytic solution at pH 7.3.

Table I
Number- and Weight-Average Diameters of P(MAA-*g*-EO) Microspheres

surfactant concn during polymern, wt %	number-average diameter, $\bar{d}_n$, μm	standard deviation, μm	weight-average diameter, $\bar{d}_w$, μm
0.0	29.5	12.7	34.9
0.1	27.1	8.5	29.8
1.0	18.4	5.7	20.2
1.5	24.8	3.4	25.2

The 1:1 w/w monomer feed ratio used to form the microparticles corresponded to a monomer molar ratio (M(1000)G/MAA) of 1:11.6. Therefore, for every M(1000)G ester repeating unit along the copolymer backbone, there were 11.6 MAA repeating units. The PEG chains with approximately 23 repeating units per chain were pendant to the polymer backbone. This stoichiometry assured formation of some blocks of PMAA with at least 11.6 repeating units per block. ^{13}C NMR investigation of similar networks[5] revealed nearly stoichiometric incorporation of both monomers into the networks and a compositional heterogeneity of the copolymer backbone (i.e., the carbonyl/carboxylate portion of the ^{13}C spectrum revealed heterogeneous trends in the monomer sequence distribution).

The particle size distribution was determined for particles prepared without surfactant and for particles prepared with 0.1, 1.0, and 1.5 wt % P(DMS-*b*-EO) as a surfactant in the suspension polymerization. The particle size distribution for particles prepared in the presence of 1.5 wt % P(DMS-*b*-EO) is shown in Figure 4.

The number- and weight-average diameters of the particles, $\bar{d}_n$ and $\bar{d}_w$, respectively, were calculated by application of the classical average equations shown in eq 1 and 2. Here, N_i is the number of particles with a certain diameter d_i.

$$\bar{d}_n = \sum_{i=1}^{n} N_i d_i / \sum_{i=1}^{n} N_i \quad (1)$$

$$\bar{d}_w = \sum_{i=1}^{n} N_i d_i^2 / \sum_{i=1}^{n} N_i d_i \quad (2)$$

The results of these calculations are tabulated in Table I and show the dependence of the average values on surfactant content. As surfactant concentration increased from zero to 1 wt %, the average particle diameter decreased; however, as the surfactant was increased to 1.5 wt %, the particle diameters increased. Because of this threshold, the surfactant concentration of 1 wt % was proposed for the suspension polymerization technique.

In addition to the effect on particle size, surfactant concentration had a significant effect on the monodispersity of the particles, as indicated by the standard deviations calculated for the number-average diameters. As surfactant concentration increased, the deviation from the average diameter decreased. This result suggests that the surfactant provides better control of the surface tension of the monomer droplets in the silicone oil.

The equilibrium degree of swelling for the microspheres was calculated from the radii data. This analysis resulted in an equilibrium degree of swelling of 8.0 at pH 4.75 and of 13.2 at pH 7.40.

Conclusion. P(MAA-*g*-EO) can be prepared in the form of microspheres by means of a free-radical suspension polymerization. These particles have a water-swollen diameter ranging from 10 to 60 μm and were found to be stable in pHs ranging from 4.75 to 7.4. In addition, increasing the concentration of the surfactant, P(DMS-*b*-EO) caused a decrease in the polydispersity of the particle size distributions.

Acknowledgment. The financial support of NSF Grant CBT 87-14653 is greatly appreciated.

Registry No. (MMA)(EO)(TEGDMA) (graft copolymer), 122093-19-0; (MMA)(TEGDMA)(M(1000)G) (graft copolymer), 122093-21-4.

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Stabilization of a Liquid-Crystalline Phase through Noncovalent Interaction with a Polymer Side Chain

Liquid-crystalline polymers have great potential as functional materials, in applications as varied as electrooptic devices or high-strength fibers.[1] It is well-known that molecular interactions have a significant influence on the ordering of liquid-crystalline states. The proper combination of the shape of a molecule and the magnitude as well as the orientation of its interactions with neighboring species contributes to the liquid crystallinity of the molecule. In the case of some liquid-crystalline carbohydrates[2] or poly(ester amides),[3] intermolecular hydrogen bonds are present and contribute to the overall order of their mesophases.

The objective of this study was to determine if a polymer containing a side-chain group capable of hydrogen bonding could be used to stabilize and enhance the mesomorphicity of a mesogenic small molecule with which it could interact through formation of hydrogen bonds. Clearly, the geometry of the two components would be critical as H bonding should occur along the long molecular axis of the two interacting species. Since H-bonding interactions are much stronger than those resulting from the more usual dipole–dipole interaction, any stabilizing influence would likely be of unusual magnitude.

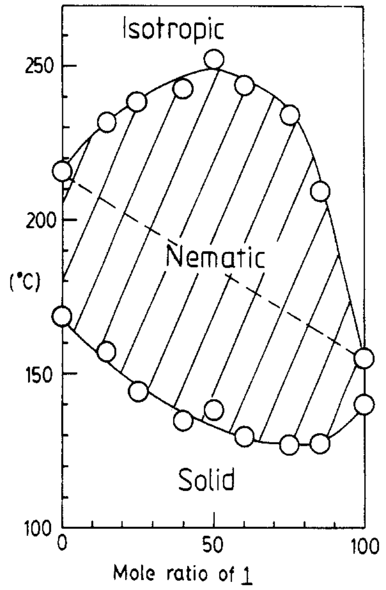
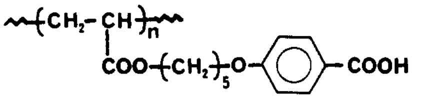


Figure 1. Phase diagram for the binary mixtures of polymer 1 and stilbazole 2.

In a first approach, the interacting moieties used were the carboxylic acid side chain of polymer 1 and the pyridine ring of a low molecular weight liquid-crystalline compound 2. Polymer 1 is a polyacrylate[4] containing in its side chain a pentamethylene spacer group terminated with a 4-oxybenzoic acid unit. Due to the formation of hydrogen bonds between its pendant pentoxybenzoic acid groups, polyacrylate 1 exhibits mesomorphicity with a nematiclike phase observed between 140 and 155 °C. Compound 2[5] is a *trans*-stilbazole ester moiety with nitrogen at the para position; 2 exhibits a nematic state between 168 and 216 °C.[6] Binary mixtures of these two components were examined since intermolecular hydrogen bonding between them should allow the complex to retain overall linearity thereby forming a new, longer rodlike mesogenic structure. In order to ensure that a regular 1:1 complex of two species is obtained, the binary mixture of 1 and 2 was prepared by slow evaporation from pyridine solution. This technique, which involves the use of an interacting solvent to break self-hydrogen bonding, has been used successfully by our laboratory in previous experiments[7,8] exploring the formation of homogeneous polymer blends with H-bond donor and acceptor polymers such as poly(4-hydroxystyrene)[7] or poly(4-vinylbenzoic acid)[8] with poly(4-vinylpyridine). As a result of H-bond formation, such polymer blends are compatible and show single T_g values appreciably higher than those of either of the individual components of the mixture because of the formation of the hydrogen-bonded complexes.



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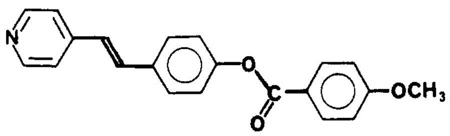

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