

## Solvent and Reagent Accessibility within Oligo(ethylene glycol) Ether [PEG] Cross-Linked Polystyrene Beads

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$\alpha,\omega$ -Bis-4(vinylbenzyl) ethers of mono-, di-, tetra-, and hexa(ethylene glycol) were used as cross-linkers in polystyrene beads to examine the influence of glycol tether length and % incorporation upon polymer swelling and reagent diffusion. Swelling of 2, 10, and 20% cross-linked poly{styrene-*co*-[oligo(ethylene glycol) bis(4-vinylbenzyl)ether]} (PS-PEG) beads was determined to be higher or comparable to 2% cross-linked poly[styrene-*co*-divinylbenzene] (2% PS-DVB) beads. Fluorescence quenching of polymer-bound dansyl groups by  $\text{Et}_3\text{O}\cdot\text{BF}_4$  indicated that the most rapid intrasite diffusion of this electrophilic reagent occurred in toluene. PS-PEG beads exhibited faster quenching than 2% PS-DVB in poor swelling solvents but were slower to quench than 2% PS-DVB in toluene.

The renaissance in solid-phase (SP) organic synthesis,<sup>1</sup> driven by small molecule combinatorial approaches to lead generation and optimization, has placed new demands on solid supports. While considerable effort has been directed toward new linker<sup>2</sup> and anchoring group<sup>3</sup> strategies to adapt existing polystyrene-divinylbenzene (PS-DVB) supports to nonpeptide type couplings and reaction sequences, less research has been directed toward modification of the PS matrix itself. Microporous PS-DVB, with its high thermal stability, chemical inertness, and mechanical robustness, is an attractive support for solid-phase synthesis. Although useful in a variety of solvents and reaction conditions, two inter-related aspects affect the performance of conventional microporous PS-DVB supports in highly polar media: (i) limited swelling and (ii) limited reagent and/or solvent accessibility. Optimized solvation of the whole polymeric matrix is considered essential in solid-phase peptide synthesis<sup>4</sup> and is likewise anticipated to be critical for the success of new reactions and synthetic sequences. Conventional microporous PS-DVB beads, e.g. Merrifield type, swell only slightly in highly polar solvents or aqueous cosolvent systems which can lead to acute diffusional limitations and/or low yields for reactions requiring these media. The design of chemically inert and mechanically hardy PS-supports possessing enhanced swelling and reagent accessibility in highly polar media represents a challenge in SP technology.

Our interest in solid-phase synthesis,<sup>5</sup> support modification,<sup>6</sup> and cross-link functionalization<sup>7</sup> prompted us to investigate the properties of oligo(ethylene glycol)

cross-linked PS beads. Poly(ethylene glycol) [PEG], introduced via grafting to chloromethylated PS-DVB, has been shown to increase swelling in polar solvents,<sup>8</sup> and several PEG-grafted PS-DVB supports have emerged (cf., TentaGel and ArgoGel)<sup>9</sup> based on the work of Inman,<sup>10</sup> Regen,<sup>11</sup> Mutter,<sup>12</sup> Bayer and Rapp,<sup>13</sup> Barany,<sup>14</sup> and others.<sup>15</sup> A drawback of the grafting approach, however, is that it reduces the functional group-to-mass ratio (polymer loading) by decreasing the number of free chloromethyl groups while increasing the resin mass. An alternative approach to postpolymerization grafting is inclusion of vinyl-functionalized PEG monomers in the copolymer formulation.<sup>16</sup> Replacing DVB with  $\alpha,\omega$ -bis-functionalized PEG as the cross-linking agent<sup>17</sup> represents a particularly intriguing approach as the properties of polymer networks are significantly influenced by the nature of the network junctions.<sup>18</sup> Recently, bis-styrene-terminated PEG<sup>19</sup> and oligo(ethylene glycol)<sup>20</sup> derived monomers were copolymerized with styrene to produce supports used for Diels-Alder catalysis and peptide

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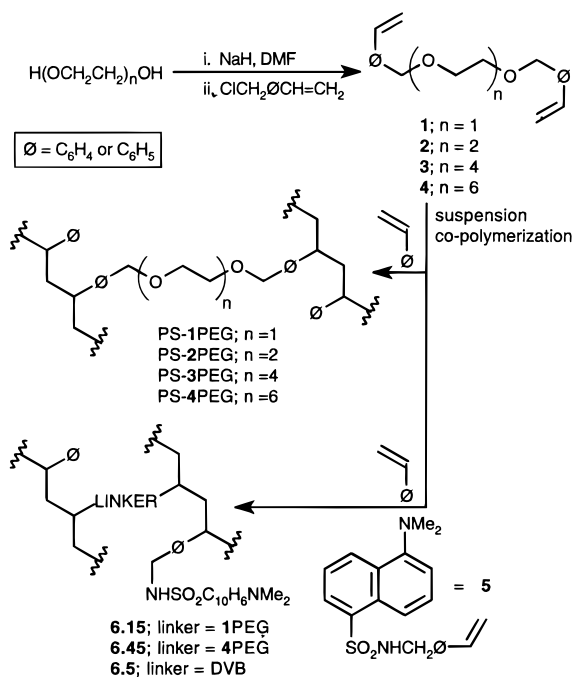
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**Scheme 1. Preparation of PEG-monomers 1–4 and Suspension Copolymerization with Styrene To Afford PS–PEG and Dansyl-Labeled PS–PEG Beads**



synthesis, respectively. These copolymers were reported to swell in polar solvents and exhibit superior mechanical properties to PS–DVB, but the specific influence of PEG tether length and mole percentage incorporation on the swelling properties of the supports was not investigated.

We report herein synthesis of PS beads cross-linked with  $\text{CH}_2=\text{CHØCH}_2(\text{OCH}_2\text{CH}_2)_n\text{OCH}_2\text{ØCH}=\text{CH}_2$  ( $n = 1, 2, 4,$  and  $6$ ) and their respective swelling and diffusive properties relative to 2% cross-linked PS–DVB. Swelling was examined by the syringe method<sup>21</sup> where the volume of beads soaked in a solvent was compared to the dry bead bed volume. The diffusive properties were examined by observing fluorescence quenching of polymer-bound dansyl by addition of triethyloxonium tetrafluoroborate according to the method of Shea et al.<sup>22</sup>

## Results and Discussion

**Monomer Synthesis and Suspension Copolymerization.** Cross-linking monomers 1–4 were prepared by bis-alkylation of commercially available mono- or oligo-(ethylene glycol)s with 4-vinylbenzyl chloride (Scheme 1). Suspension copolymerization with styrene was accomplished according to a preparative-scale (100–500 g beads) procedure described in another publication<sup>7</sup> to afford beads (100–500  $\mu\text{m}$  diameter) in 86–100% yield. These were used in the swelling assays. For the fluorescence quenching experiments, smaller (30–150  $\mu\text{m}$  diameter) beads (**6**) having  $7.9 \times 10^{-4}$  mmol/g of dansyl monomer **5**<sup>23</sup> in the formulations were prepared in 47–100% yield according to a microscale (1–10 g beads) procedure developed in our laboratory. All beads are

identified with the descriptor “#”% PS-“X”, where “#”% indicates the cross-link density in terms of the mass percent of DVB required to give the corresponding mole percentage of cross-linker in the formulation; “X” indicates the cross-linker used (DVB or monomers 1–4, referred to collectively as “PEG”). Thus, a copolymer cross-linked with **4** having the same mole % cross-linker as 2% (w/w) DVB cross-linked PS (i.e., 2% PS–DVB) is designated by 2% PS-**4**PEG.

**Solvent Swelling Assays.** A common parameter in the study of polymer solvation is the Hildebrand solubility parameter.<sup>24</sup> This is the square-root of the cohesive energy density (the energy per unit volume required to separate the molecules in a system against no opposing pressure) and is related to the enthalpy of mixing of a polymer–solvent pair through:

$$\Delta H_{\text{mix}} = n_1 V_1^\circ \phi_2 (\delta_1 - \delta_2)^2 \quad (1)$$

where  $\delta_1$  and  $\delta_2$  are the solubility parameters of solvent and polymer, respectively. The variable  $n_1$  is the number of moles of solvent,  $V_1^\circ$  is the molar volume of the solvent, and  $\phi_2$  is the volume fraction of the polymer. As the value of  $\delta$  for polymer and solvent approach one another,  $\Delta H_{\text{mix}}$  decreases. Since the free-energy of mixing decreases with  $\Delta H_{\text{mix}}$  (the entropy of mixing is almost always positive), systems that mix with small enthalpies are expected to have high miscibility. For cross-linked polymers, this corresponds to increased swelling. In practice, solvents that are considered “good” swelling solvents have a solubility parameter within 2–3  $\text{MPa}^{1/2}$  of the polymer. Accordingly, good swelling solvents for lightly cross-linked PS–DVB (solubility parameter = 18.5  $\text{MPa}^{1/2}$ )<sup>25</sup> are methylene chloride (19.9), THF (19.1), and toluene (18.2). Dimethylformamide (24.7), diethyl ether (15.1), and ethanol (26.2) are medium to poor swelling solvents.

We examined the swelling ratios of these PS–PEG copolymers in solvents over a range of solubility parameters to establish whether their response curves were roughly similar to PS–DVB and whether the PEG tether length affected the extent of swelling. Figure 1 reveals that while PS–PEG copolymers swelled more than 2% PS–DVB, the overall trend in swelling was the same regardless of the cross-linker used. Maximum swelling was observed in toluene with less swelling in solvents that deviated from the regime near 18  $\text{MPa}^{1/2}$ . Interestingly, the swelling behavior of the 2% PS–PEG beads did not appear to be a function of PEG tether length (2% PS-1PEG  $\approx$  2% PS-2PEG  $\approx$  2% PS-3PEG  $\approx$  2% PS-4PEG). Presumably, at the 2% incorporation level the PEG units have little synergistic influence upon the swelling properties of the beads. At a higher level of incorporation, i.e., 20% PEG (Figure 2), however, swelling increased with increased PEG tether length. Not surprisingly, the swelling properties of PS-4PEG depended heavily on the cross-link density (Figure 3). It is interesting to note that 20% PS-4PEG swelled nearly as much as 2% PS–DVB!

We measured bead swelling in THF–water mixtures (Figure 4) to determine if PEG tether length influenced swelling in this aqueous cosolvent and found that both DVB and PEG cross-linked beads showed nearly identical

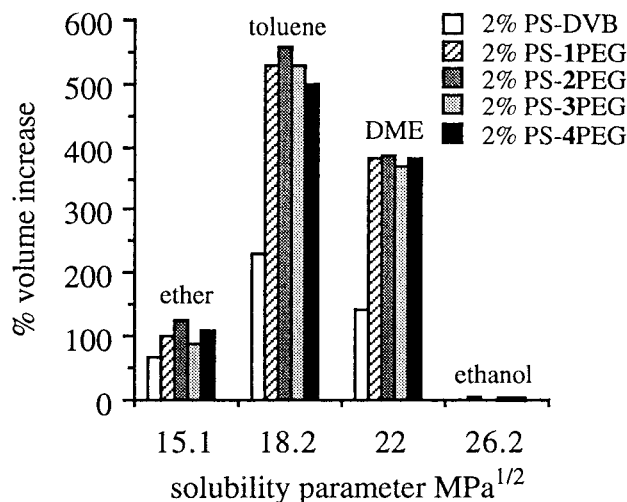
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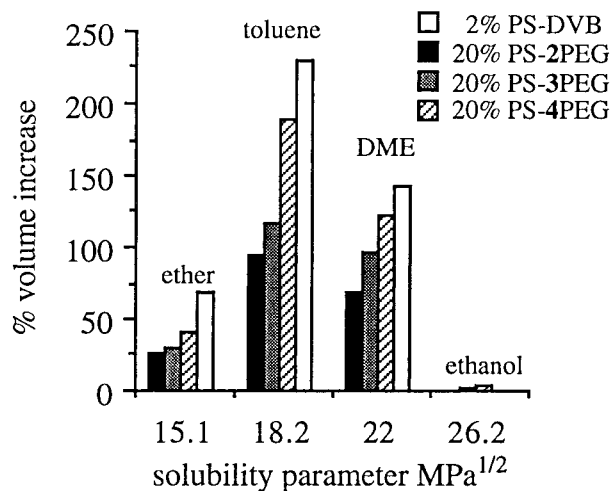
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**Figure 1.** Swelling by 2% PS-DVB and 2% PS-PEG beads in various solvents as a function of solvent solubility parameter. DME = dimethoxyethane.



**Figure 2.** Swelling of 2% PS-DVB vs 20% PS-PEG beads in various solvents as a function of solvent solubility parameter.

swelling below 50% THF. Indeed, as the THF composition dropped from 50%, all four 2% cross-linked resins showed little swelling. Increasing the THF concentration toward 100% resulted in increasingly impressive swelling of the 2% PS-PEG resins.

#### Diffusion Studies via Fluorescence Quenching.

The diffusive properties of polymer supports can profoundly influence the kinetics of a solid-phase reaction.<sup>26</sup> In microporous beads, where pore size depends on swelling, reaction rates tend to increase with swelling<sup>27</sup> and decrease with cross-link density.<sup>28</sup> Ford, who studied self-diffusion of solvents<sup>29</sup> and small molecules<sup>30</sup> in lightly cross-linked PS-DVB using pulsed-field-gradient spin-echo (PGSE) NMR, observed lower self-diffusion con-

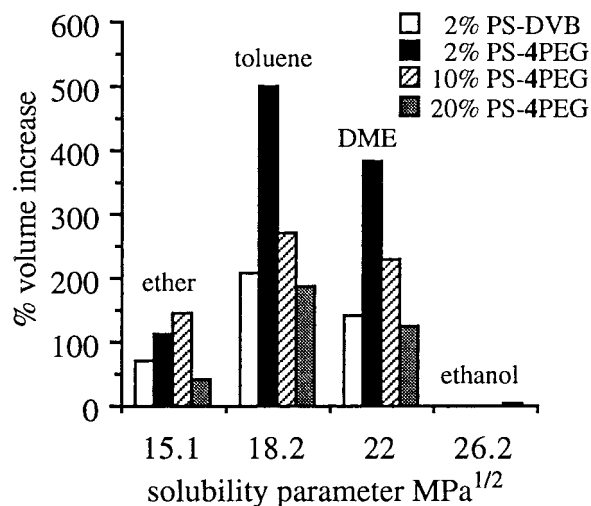
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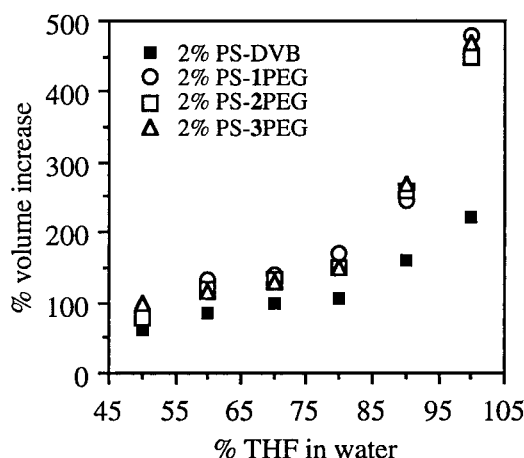
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**Figure 3.** Swelling of 2% PS-DVB vs 2%, 10%, and 20% PS-4PEG beads in various solvents as a function of solvent solubility parameter.



**Figure 4.** Swelling of 2% PS-DVB vs 2% PS-PEG beads in THF-water.

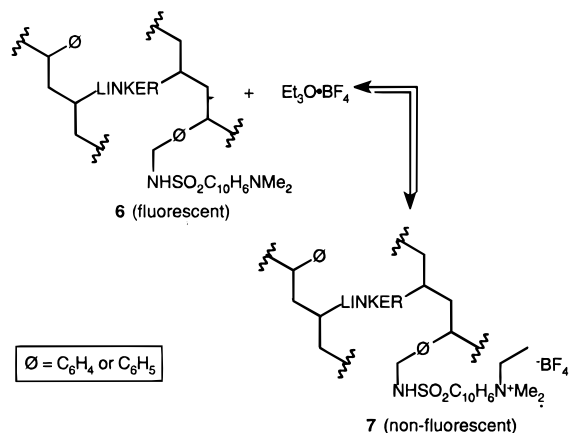
stants with decreasing swelling ratios. This has been attributed to diffusional constraint imposed by network collapse and/or obstruction effects arising as diffusants travel around the impermeable and relatively immobile matrix elements. Because the introduction of PEG units at the cross-links of PS beads was found to improve swelling, we anticipated that enhanced mass transport would also be observed.

The diffusive properties of these beads were examined by following the time course of triethyloxonium tetrafluoroborate ( $\text{Et}_3\text{O}^+\text{BF}_4^-$ ) fluorescence quenching of covalently bound dansyl groups (see **6** in Scheme 1). This quenching reaction, involving reversible<sup>31</sup> quaternization of the dansyl dimethylamino moiety in **6** giving **7** (Scheme 2),<sup>32</sup> is extremely rapid. Since the analogous solution-phase quenching of monomer **5** was virtually instantaneous (<1 s), the diminution of fluorescence intensity reflects the diffusion of  $\text{Et}_3\text{O}^+\text{BF}_4^-$  into the beads. Shea et al. used this method as a measure of polymer permeability in PS-DVB resins,<sup>22</sup> and Morawetz used this method to esti-

(31) The reversibility of the reaction was verified in that addition of ca. 5 equiv (with respect to  $\text{Et}_3\text{O}^+\text{BF}_4^-$ ) of triethylamine completely restored the fluorescence intensity to its original value.

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**Scheme 2. Reversible Quaternerization of the Dansyl Group in 6 Causing Fluorescence Quenching. The Alkylated Dansyl Group in 7 Absorbs at Shorter Wavelength, Diminishing the Extinction Coefficient at the Excitation Wavelength (340 nm)**



mate (pseudo) first-order rate constants for diffusion-with-reaction in various polymers.<sup>33</sup> Here, we use fluorescence quenching as a model reaction on the solid-phase that can be easily monitored and is rapid enough to reflect the diffusive properties of the beads.

Examination of the fractional uptake<sup>34</sup> of  $\text{Et}_3\text{O}\cdot\text{BF}_4$  by dansyl-functionalized 2% **6.45** in various solvents (Figure 5) suggests a relationship exists between the thermodynamic quality of the solvent and the rate and/or mode of diffusion. Copolymer **6.45** (Figure 5a) showed similar quenching rates in ether and acetonitrile, but faster quenching rates in toluene. The dansyl-functionalized 2% **6.5** (Figure 5b) showed a more pronounced solvent dependence with decreasing quenching rates in the order toluene > DME > ether > acetonitrile. Evident in all sorption curves was a slight concavity toward the  $t^{1/2}$  axis, particularly in diethyl ether. While purely Fickian diffusion gives linearity up to 0.5–0.8 fractional uptake, curvature below 0.5 is typically associated with pseudo-Fickian behavior. Accordingly, diffusion within the beads may not always be a function of diffusant concentration only (i.e., purely Fickian), but could also depend on other variables.

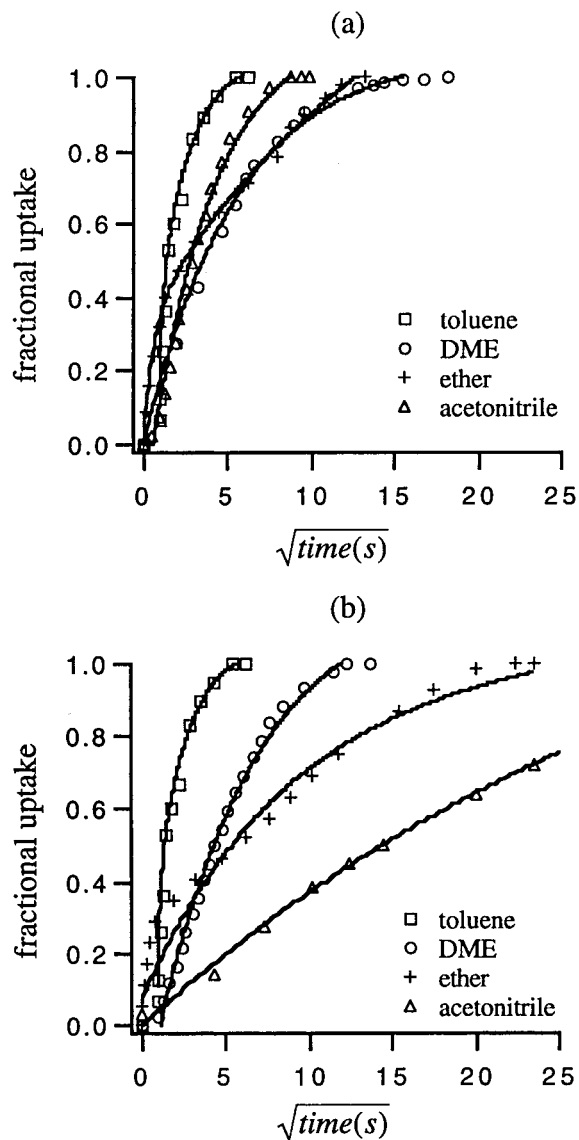
To further understand the relationship between solvent quality and the diffusive properties of the beads, the half-lives for fluorescence quenching of 2, 10, and 20% **6.45** were plotted as a function of solvent solubility parameter (Figure 6). As pointed out above, the rates of fluorescence quenching were greatest in toluene, a high swelling solvent. The quenching rates of 2% **6.5** followed a trend toward increased diffusivity in better swelling solvents. The quenching rate of **6.45**, on the other hand, appeared to be less of a function of solvent quality. For example, while swelling in acetonitrile was negligible for both polymer types, 2% **6.45** showed significantly faster quenching rates than 2% **6.5** in this solvent.

(33) Pan, S.-S.; Morawetz, H. *Macromolecules* **1980**, *13*, 1157.

(34) The fluorescence intensity ( $I$ ) can be correlated to the fractional uptake ( $M_s^t/M_s^\infty$ ) of  $\text{Et}_3\text{O}\cdot\text{BF}_4$  within the beads, through the expression:

$$\frac{M_s^t}{M_s^\infty} = \frac{I_{\text{init}} - I_t}{I_{\text{init}} - I_{\text{final}}}$$

with the proviso that the partition coefficient between the bead and the solvent phases is unity.

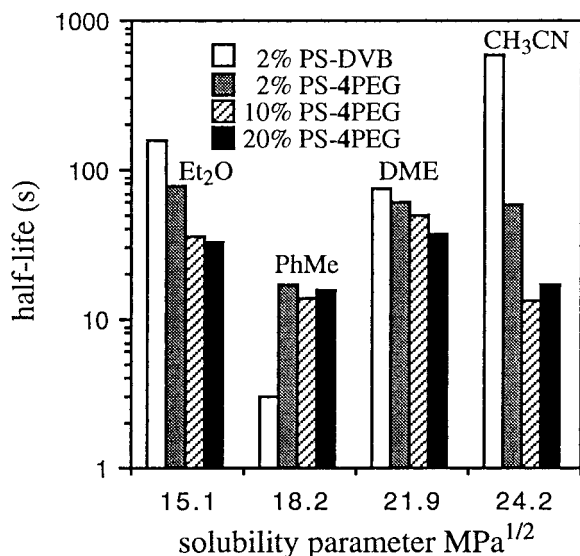


**Figure 5.** Fractional uptake of  $\text{Et}_3\text{O}\cdot\text{BF}_4$  as a function of  $t^{1/2}$  for polymers: (a) 2% PS-4PEG and (b) 2% PS-DVB. The curves are the corresponding least-squares best fits.

The significantly higher half-lives observed for **6.45** relative to **6.5** in toluene seems counterintuitive, considering that swelling of these resins was higher or comparable to 2% PS-DVB. However, reagent diffusion and even the quenching reaction itself can be influenced by the topographical (location of dansyl groups within the matrix) and topochemical (microenvironment) properties of the networks.<sup>35</sup> There are likely to be microstructural differences between PS-4PEG and PS-DVB networks. PS-DVB is known to be heterogeneously cross-linked with dense microgel and/or aggregate regions dispersed within lighter cross-linked regimes.<sup>36</sup> Swelling of the denser microregions is minimal so the majority of swelling within PS-DVB is accounted for by the chains in the interstitial (between clusters) regime. Thus, the diffusing species will encounter a less cross-linked interstitial phase than would be the case in a more uniformly cross-linked network.<sup>37</sup>

(35) Morawetz, H. *J. Macromol. Sci. Chem.* **1979**, *A13*, 311.

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**Figure 6.** Fluorescence quenching half-lives of 2% PS-DVB vs 2%, 10%, and 20% PS-4PEG beads as a function of solvent solubility parameter. These  $t_{1/2}$  are averages of three quenching experiments.

Reagent diffusion can also be reduced by interactions of the diffusant with the polymer matrix, e.g. hydrogen bonding, dipole attraction, or complexation. While PS itself could interact weakly with  $\text{Et}_3\text{O}\cdot\text{BF}_4$ , the PEG moieties can form stronger ion-dipole interactions or even oxonium species via alkylative transfer that would lower the concentration of  $\text{Et}_3\text{O}\cdot\text{BF}_4$  free to diffuse. It should be noted that the differences between the quenching times of **6.45** and **6.5** beads were the least in DME (a medium anticipated to level "matrix interaction" effects arising from the PEG moieties).

The effect of cross-linking and/or PEG incorporation on the rates of quenching can also be seen in Figure 6. While the 2% **6.45** and 20% **6.45** beads appeared to have similar quenching rates in toluene, the influence of cross-linking was more pronounced in less swelling solvents. The 2% **6.45** beads were consistently slower to quench in poor swelling solvents than the higher cross-linked **6.45** resins. Whether this is due to microstructural differences between the light and heavy cross-linked networks or from other factors is not known.

To examine the influence of PEG tether length at constant cross-linking, 2% **6.15** and 2% **6.45** were quenched in dimethoxyethane (DME). The quenching was carried out in this medium to level any "matrix interactions" as discussed above. The half-lives for fluorescence quenching were the same within experimental error (62 and 58 s, respectively). This was consistent with the swelling data that showed the two resins to have essentially the same swelling in DME (379 and 380%, respectively).

It is informative to compare the half-lives obtained in the present study with values reported for similar quenching studies. In Shea's report of fluorescence quenching resins labeled with **5**,<sup>22</sup> the half-lives for

quenching of 5% and 20% cross-linked PS-DVB particles (125–150  $\mu\text{m}$ , in  $\text{CH}_2\text{Cl}_2$ /hexane, 13:4) were ca. 25 and 35 s, respectively. Morawetz<sup>35</sup> reported the half-life for fluorescence quenching of a 4-(dimethylamino)styrene labeled 3% cross-linked butyl methacrylate-*co*-ethylene dimethacrylate beads swollen in cyclohexane was 870 s. Thus, the fluorescence quenching data obtained in the present study is comparable to literature data and has provided some insights into the diffusive properties of PS-PEG microbeads relative to conventional PS-DVB.

**Conclusions.** Installation of  $\alpha,\omega$ -bis(4-vinylbenzyl) ethers of mono-, di-, tetra-, and hexa(ethylene glycol) at the cross-links of PS beads was found to improve swelling in polar solvents and THF-water mixtures over 2% PS-DVB. Fluorescence quenching of dansyl labeled beads by  $\text{Et}_3\text{O}\cdot\text{BF}_4$  indicated that the most rapid intrasens diffusion of this reagent occurred in toluene. PEG cross-linked beads exhibited smaller half-lives for fluorescence quenching than 2% PS-DVB in the poor swelling solvents but were slower to quench than PS-DVB in toluene (a good swelling solvent). The length of the oligo-(ethylene glycol) tethers, while influencing the extent of bead swelling in several solvents in 20% PS-PEG, did not appear to effect fluorescence quenching rate in DME.

## Experimental Section

All general procedures and instrumentation are identical to those listed in another publication.<sup>7</sup>

**1,2-Bis(4-vinylbenzyloxy)ethane (1).** Into a 100 mL round-bottom flask was placed dry DMF (40 mL) and double-distilled ethylene glycol (1.24 g, 20 mmol). NaH (1.84 g; 60% w/w in mineral oil, 46 mmol; hexane washed to remove oil) was slowly added to the rapidly stirring solution, and the reaction was stirred at room temperature for 1 h. The flask was immersed in a cold water bath (10 °C), and 4-vinylbenzyl chloride (7.05 g, 46 mmol) was added dropwise so as to keep the temperature of the reaction below 25 °C. Nitrobenzene (10 mg, to inhibit polymerization) was added, and the mixture was stirred in the dark at room temperature for 24 h. The DMF was removed in vacuo at 50 °C to ca. 15 mL of solution. Water (100 mL) was added, and the solution was extracted three times with 75 mL of diethyl ether. The combined ether extracts were concentrated in vacuo, to give a light yellow oil that was purified by flash column chromatography on silica gel using 20:80 ethyl acetate:hexanes to afford 4.0 g (68%) of **1** as a crystalline solid. <sup>1</sup>H NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  3.64 (s, 4H), 4.56 (s, 4H), 5.23 (d, 2H,  $J = 10.8$  Hz), 5.73 (d, 2H,  $J = 17.6$  Hz), 6.70 (dd, 2H,  $J = 17.6, 10.8$  Hz), 7.30 (d, 4H,  $J = 8.1$  Hz), 7.38 (d, 4H,  $J = 8.1$  Hz); <sup>13</sup>C NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  69.37, 72.81, 113.56, 126.07, 127.75, 136.44, 136.81, 137.81. IR (neat) 3086, 1630, 1091  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{20}\text{H}_{22}\text{O}_2$ : C, 81.60; H, 7.53. Found: C, 81.47; H, 7.60. HRMS calcd for  $\text{C}_{20}\text{H}_{22}\text{O}_2$  294.1620. Found 294.1642.

**Di(ethylene glycol) Bis(4-vinylbenzyl) Ether (2).** The reaction was carried out as described for **1** using 200 mL of DMF, 37.90 g (248.4 mmol) of 4-vinylbenzyl chloride, 10.80 g (248.4 mmol) of NaH, and 11.46 g (108 mmol) of di(ethylene glycol). Purification by flash column chromatography on silica gel afforded 21.1 g (58%) of **2** as an oil. <sup>1</sup>H NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  3.65 (m, 8H), 4.55 (s, 4H), 5.22 (d, 2H,  $J = 10.9$  Hz), 5.73 (d, 2H,  $J = 17.6$  Hz), 6.73 (dd, 2H,  $J = 17.6, 10.9$  Hz), 7.29 (d, 4H,  $J = 8.1$  Hz), 7.37 (d, 4H,  $J = 8.1$  Hz); <sup>13</sup>C NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  69.06, 70.25, 72.42, 113.21, 125.76, 127.41, 136.15, 136.42, 137.59; IR (neat) 3086, 1630, 1101  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{22}\text{H}_{26}\text{O}_3$ : C, 78.07; H, 7.74. Found: C, 77.97; H, 7.93. HRMS calculated for  $\text{C}_{22}\text{H}_{26}\text{O}_3$ : 338.1882. Found: 338.1861.

**Tetra(ethylene glycol) Bis(4-vinylbenzyl) Ether (3).**<sup>17</sup> The reaction was carried out as described for **1** using 40 mL of DMF, 6.71 g (43.9 mmol) of 4-vinylbenzyl chloride, 1.84 g

(37) This assumes that the use of isomerically pure cross-linking agents **1–4** affords more homogeneously cross-linked networks than PS cross-linked with DVB (a mixture of 3- and 4-isomers). Even so, differences between the reactivity ratios of the DVB isomers relative to monomers **1–4** are likely to result in different distributions of cross-links within the DVB and PEG cross-linked networks.

(46.2 mmol) of NaH, and 3.88 g (19.9 mmol) of tetraethylene glycol. Purification by flash column chromatography on silica gel afforded 5.13 g (60%) of **3** as an oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  3.57–3.60 (br m, 4H), 3.64 (br s, 12H), 4.51 (s, 4H), 5.2 (d, 2H,  $J = 12$  Hz), 5.71 (d, 2H,  $J = 18$  Hz), 6.67 (d, 2H,  $J = 18$ , 9 Hz), 7.27 (d, 4H,  $J = 8.1$  Hz), 7.35 (d, 4H,  $J = 8.1$  Hz);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  69.19, 70.41, 72.67, 113.48, 125.96, 127.67, 136.32, 136.68, 137.70; IR (neat) 2883, 1630, 1103  $\text{cm}^{-1}$ .

**Hexa(ethylene glycol) Bis(4-vinylbenzyl) Ether (4).** The reaction was carried out as described for **1** using 40 mL of DMF, 4.66 g (30.5 mmol) of 4-vinylbenzyl chloride, 1.40 g (35.0 mmol) of NaH, and 3.92 g (13.88 mmol) of hexaethylene glycol. Purification by flash column chromatography on silica gel afforded 4.68 g (66%) of **4** as a light yellow oil.  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  3.63–3.65 (br m, 24 H), 4.54 (s, 4H), 5.22 (d, 2H,  $J = 10.8$  Hz), 5.73 (d, 2H,  $J = 17.6$  Hz), 6.70 (dd, 2H,  $J = 17.6$ , 10.8 Hz), 7.29 (d, 4H,  $J = 8.2$  Hz), 7.38 (d, 4H,  $J = 8.2$  Hz);  $^{13}\text{C NMR}$  (75 MHz,  $\text{CDCl}_3$ )  $\delta$  68.7, 69.8, 69.9, 72.1, 112.9, 125.5, 127.1, 135.9, 136.1, 137.3; IR (neat) 2865, 1630, 1103  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{30}\text{H}_{42}\text{O}_7$ : C, 70.01; H, 8.23. Found: C, 69.93; H, 8.28. HRMS calculated for  $\text{C}_{30}\text{H}_{42}\text{O}_7$ : 514.2919. Found: 514.2961.

**Microscale Suspension Copolymerizations.** Into a 100 mL ground glass-flanged reaction flask (Kontes 296100–0100) with matching three-neck top (Kontes 296-170-0000) and floating magnetic stir bar [encapsulated Alnico-V magnet and bar fluoropolymer bracket; 21/8 in.  $\times$  11/8 in. (Nalgene 6630-0250)] were added water (150 mL), poly(vinyl alcohol) (1 g), and NaCl (3.75 g). The flask was sealed, lowered into an 85  $^\circ\text{C}$  oil bath, and purged with  $\text{N}_2$  for 1 h. The suspended phase, consisting of cross-linker (extracted free of inhibitor *tert*-butyl cachetol), styrene (see Table 1 in Supporting Information for formulations), benzoyl peroxide, and 2.3 g of a 0.254 mg/mL solution of dansyl monomer **5**<sup>23</sup> in 10:90 THF:toluene, was added to the rapidly stirring continuous phase. Vigorous stirring was continued for 2 h and then slowed to a minimum for the duration of the polymerization (24 h total). The slurry of beads was filtered through a coarse-sintered glass funnel and washed with 50 mL each of 10% aqueous HCl, water, 10% aqueous NaOH, water, 10% aqueous NaOH, water, THF, ether, methanol, ether, and hexanes. The beads were air-dried for 0.5 h and then placed in a vacuum oven at 45  $^\circ\text{C}$  overnight. Dry sizing of the beads was accomplished using a sonic sifter (ATM Corp., Milwaukee, WI) through 125, 106, 75, 45, and 20  $\mu\text{m}$  sieves.

**Swelling Assays.** Polymer beads (2 g, 100–300  $\mu\text{m}$  diameter) were placed in a 12  $\text{cm}^3$  graduated polyethylene–polypropylene syringe with a plug of cotton in the tip to

prevent bead passage. The syringe was affixed vertically by insertion of the needle into a rubber stopper, and the side of the syringe was tapped several times to ensure close packing of the beads. The dry volume was recorded, and solvent was added through the top of the syringe. The beads were equilibrated in the solvent for 0.5 h with occasional stirring with a fine wire to remove air bubbles. The side of the syringe was tapped, and the volume was recorded. Solvent was removed by suction, and the beads were rinsed three times with the next solvent with 20 min intervals between solvent removal and reintroduction. The beads were equilibrated with the new solvent for 0.5 h, the syringe was tapped, and the new bed volume was recorded. All assays were performed in triplicate.

**Quenching Assays.** The fluorescence spectrometer was used in time drive mode with data collection every 0.6 s at 0.5 s per data point. The emission and excitation slits were varied to give initial signal outputs within the 600–800 AU (arbitrary units) range. Typical limits were excitation slit = 3.5–6 nm and emission slit = 5–15 nm. Excitation was at 340 nm, and observation (emission) was adjusted to the observed maximum of the given polymer–solvent pair. Polymer (20 mg, 75–45  $\mu\text{m}$  sieved) was placed into a cylindrical 4 mL borosilicate vial along with a circular magnetic stir bar. Solvent (3 mL) was added, and the vial was sealed with a rubber septum. After equilibrating at least 0.5 h, the vial was placed into the sample chamber of the spectrometer. Rapid stirring via a magnetic stirrer under the sample chamber resulted in observable fluorescence that was reasonably constant ( $\pm 5\%$  AU). Data collection was initiated, and  $\text{Et}_3\text{O}\cdot\text{BF}_4$  (20–25  $\mu\text{L}$ , 1 M in methylene chloride) was added through the septum with a 50  $\mu\text{L}$  syringe. All quenching assays were performed in triplicate.

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**Supporting Information Available:** Synthetic procedure for monomer **5** and its precursor 4-vinylbenzylamine; diagram of microscale suspension apparatus; table of representative formulations and yields for beads prepared via the microscale procedure; representative fluorescence quenching time-course for microbeads treated with  $\text{Et}_3\text{O}\cdot\text{BF}_4$  (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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