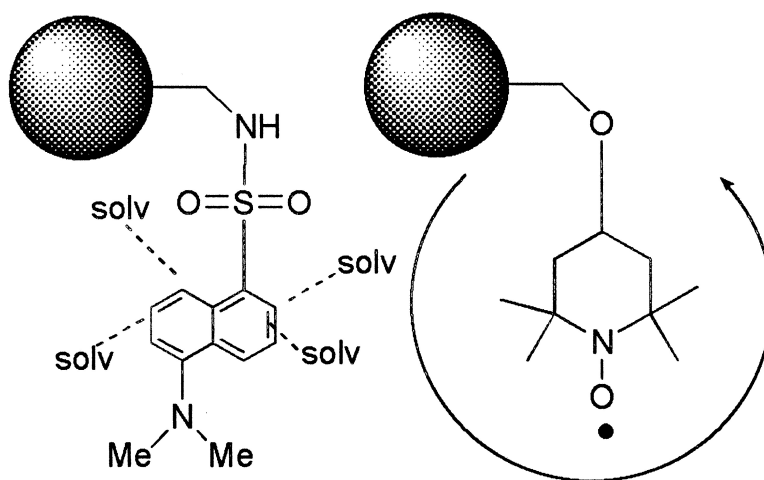


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Investigating Resins for Solid Phase Organic Synthesis: The Relationship between Swelling and Microenvironment As Probed by EPR and Fluorescence Spectroscopy

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The relationship between observed swelling of two cross-linked polystyrene resins and the microenvironment within polymer matrixes has been examined. Polystyrene cross-linked with either divinyl benzene (Merrifield resin) or 1,4-bis(4-vinylphenoxy)butane (JandaJel) was investigated with fluorescence and electron-paramagnetic resonance spectroscopy. Fluorescence spectroscopy revealed a superior correlation between observed swelling and solvation effects using a dansyl probe with JandaJel than with Merrifield resin. However, the internal viscosity of pre-swollen JandaJel is higher than Merrifield resin, as determined by EPR measurements. The combination of these two analytical methods provides insights into the physical differences observed between these two chemically similar resins and suggests caution should be used if using singular physical techniques to probe the microenvironment of polymeric matrixes.

Introduction

Peptide synthesis was irrefutably altered by the introduction in 1963¹ of polymer supports on which peptide sequences could be readily formed and even more readily isolated. With the advent of small molecule combinatorial chemistry² in the early 1990s, interest in the use of solid phase organic synthesis (SPOS) has continued to increase. The advantages of SPOS are self-evident: the ability to drive reactions to completion through the use of large excesses of reagents and ease of product isolation. A variety of linkers have been developed for the attachment of molecules to, and subsequent cleavage of molecules from, the polymeric support.³ However, the polymeric support used, namely styrene cross-linked with divinyl benzene, has remained nearly constant. Poly(styrene-*co*-vinylbenzyl-chloride-*cross*-divinylbenzene), commonly referred to as Merrifield resin (MR), has remained the solid support of choice owing to its compatibility with a wide range of reaction conditions.⁴ Recently we have introduced a polystyrene-based resin cross-linked with tetrahydrofuran, the so-called JandaJel (JJ)⁵ [poly(styrene-*co*-vinylbenzyl-chloride-*cross*-1,4-bis(4-vinylphenoxy)butane)] (Figure 1).⁶

An interesting feature of JJ is its tremendous swelling properties. Measurement of changes in volume-per-gram in 1,4-dioxane, THF, DMF, benzene, and dichloromethane revealed that JJ resin swells to at least double the volume of the corresponding MR. In fact, swelling of 2% cross-linked JJ is greater than 1% cross-linked MR in all solvents. While swelling of a gel-like resin is considered a prerequisite for facilitating reactions to occur within the solid support,⁷ it is not in itself a panacea. As the polymer swells, it now assumes

the role traditionally associated with the solvent, that is, the swollen polymer *is* the solvent, with the important distinction of having a substantially greater viscosity. Indeed, it has been shown that the kinetics of reactions on polymer supports is not always proportional to a resin's swelling capacity.⁷ A variety of spectroscopic tools have been used to examine the internal environments of cross-linked polymers and help predict reactivity, for example: small-angle neutron scattering,⁸ NMR,⁹ circular dichroism,¹⁰ and infrared spectroscopy.¹¹ Progress in analytical methods has been summarized in a recent review.¹²

In view of the development and application of JJ in the solid phase organic synthesis field,¹³ we were particularly interested in investigating the relationship between swelling and chemical reactivity and comparing the results with other commercially available supports. In the present study two spectroscopic tools, electron-paramagnetic resonance spectroscopy (EPR) and fluorescence spectroscopy, have been employed to probe the microenvironment of JJ and MR. The combination of these two methods provided unexpected results allowing new insights into the microenvironment of polymer supports.

Results and Discussion

Hildebrand Solubility Parameter and Swelling Ability.

The swelling properties of 2% cross-linked JJ (2) are remarkable given its small structural differences from MR (1). The thermodynamics of mixing (swelling in the case of a cross-linked polymer) of a polymer with a solvent is governed by the enthalpy of mixing which varies as the difference in molar attractiveness between solute and solvent.¹⁴ For a cross-linked polymer, the degree of swelling is described by the Flory–Rehner theory.¹⁵ Here, the swelling ability of a gel in a specific solvent is estimated by

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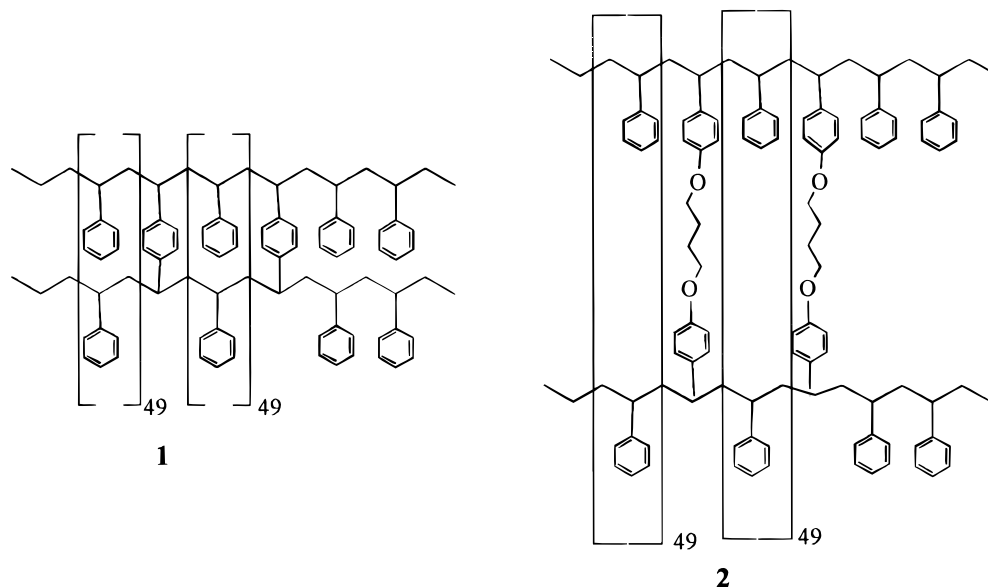


Figure 1. Depiction of Merrifield resin (1) and JandaJel (2).

comparison of the differences in Hildebrand solubility parameters (δ)¹⁶ between polymer and solvent. For a polymer, δ may be estimated from eq 1¹⁷

$$\delta = \rho \sum G/M \quad (1)$$

where ρ is the density of the polymer, M is the MER molecular weight of the polymer, and $\sum G$ is the sum of group molar attractivities; G is calculated based on experimentally determined values for vapor pressure and heats of vaporization.

Values for δ were calculated and found to be 9.4 (cal/mL)^{1/2} and 10.4 (cal/mL)^{1/2}, for 2% cross-linked JJ and MR, respectively. Recent details¹⁸ concerning δ for Merrifield resin have quoted a value of 9.1 (cal/mL)^{1/2} using¹⁹ an experimental determination of δ for linear polystyrene by a turbidimetric titration. In fact, this report gives two different values (9.07 and 8.72) for δ , depending on which solvents were employed in the titration. An alternate publication concerning δ for linear polystyrene provides a value of 8.56 (cal/mL)^{1/2}.²⁰ A range of 8.6–9.7 (cal/mL)^{1/2} has been suggested for cross-linked polystyrene.²¹

While the calculation of δ (vide supra)²² is not completely rigorous, it gives an approximation of the ability of the species to swell. In general, polymers are considered miscible when $\delta_1 - \delta_2 < 1$.²³ There are several examples where the calculation of δ for a cross-linked polymer was found to be within 10% of experimentally determined values, for example, in cross-linked polyesters,²⁴ in epoxy networks,²⁵ and in vinyl ester networks.²⁶ Thus, that the degree of swelling is enhanced greatly for JJ relative to MR is somewhat surprising, particularly when the δ values²⁷ for solvents commonly employed in SPOS are considered: for 1,4-dioxane $\delta = 10.0$ (cal/mL)^{1/2}, THF $\delta = 9.1$ (cal/mL)^{1/2}, DMF $\delta = 12.1$ (cal/mL)^{1/2}, benzene $\delta = 9.2$ (cal/mL)^{1/2}, dichloromethane $\delta = 9.7$ (cal/mL)^{1/2}. It is interesting to note that even for solvents that are more closely matched in terms of δ to MR, the swelling of the JJ is greater.

Electron-Paramagnetic Resonance Spectroscopy. The use of EPR for probing the microenvironment of large

molecules has been used for decades,²⁸ and the use of nitroxide spin labels has similarly been reported for polymers, both linear²⁹ and cross-linked.³⁰ Pioneering studies in the application of EPR to the study of MR were reported by Regen.^{30b,c,e} Regen covalently attached a nitroxide probe to MR and observed changes in τ_c . It was noted that as solvation of the resin decreased, for example, by increasing the degree of cross-linking, the mobility of the probe decreased. Changes in the line widths of the EPR signals provide a measure of the degree to which the probe is rotating in the swollen polymer. Introduction of a TEMPO spin label via radical polymerization of 4-methacryloyloxy-2,2,6,6-tetramethylpiperidine-1-oxyl has been achieved.³¹ However, it should be noted that this methodology can significantly alter the polymer matrix by introducing extra cross-linking. Hence, this method of incorporation of the spin label was not suitable for the present study where the nature of the cross-linker and its effects on resin swelling were under investigation. Thus, three preformed resins were synthetically modified by addition of a nitroxide probe.^{30c} The resins studied were 1% cross-linked MR, 2% cross-linked MR, and 2% cross-linked JJ.

Differences in the line widths of the three lines characteristic of the TEMPO spin label result from anisotropic tumbling of the radical (Figure 2). A nitroxide radical freely tumbling in solution will have an EPR spectrum with three lines of identical width. The EPR spectra of 2% cross-linked JJ under three different conditions are presented in Figure 3. The similarity of the spectrum in ethanol, a nonsolvent for JJ, to the spectrum of the dry polymer depicts the lack of any interaction. Similarly, that the spectrum in dichloromethane is so well resolved is a testament to the excellent swelling of the resin in this solvent.

Correlation time (τ_c) is loosely defined as the time required for the radical to make an arc of 40°.²⁸ Correlation times calculated from the line widths of EPR spectra of the three spin label modified resins, after swelling in a range of solvents, are shown in Figure 4. Correlation times were

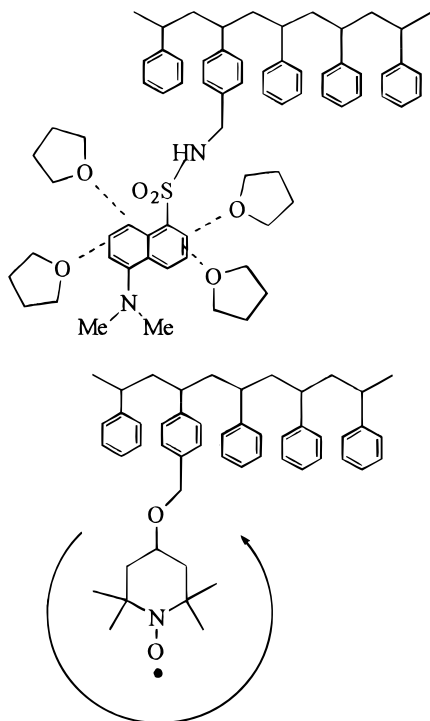


Figure 2. A drawing depicting the action of the fluorescent and radical probe attached to the polymeric support. The curved arrow signifies rotation of the radical probe.

calculated from differences in line widths according to eq 2,³²

$$\tau_c = (W_1 - W_{-1})(-15\pi\sqrt{3/8b\Delta\gamma H}) \quad (2)$$

where W_1 and W_{-1} are the leading and trailing line widths, $b = 3.06 \times 10^8$ s, $\Delta\gamma = 4.22 \times 10^4$ s⁻¹ gauss⁻¹, and H is the laboratory field. One of the limits of the above relationship between line width and τ_c is that it only holds for well-defined spectra. Thus, for broad spectra, as is obtained for the dry resin or the resin in a poor swelling solvent, excessive line-broadening precludes determination of τ_c in this manner.

Much emphasis has been placed on correlation times obtained from EPR spectra in the study of polymeric resins. In fact, a relationship between correlation time and intrinsic viscosity of the swollen polymer, $\tau_c \cong \eta T$, has been suggested.^{33,34} Previous studies on cross-linked polystyrene have demonstrated that as the degree of cross-linking increases, the mobility of the radical species decreases.³⁰ The present study shows that 2% cross-linked MR was found to have a faster τ_c than 1% cross-linked Merrifield resin in either dichloromethane or toluene. The kinetics of several reactions on 1% cross-linked Merrifield resin have also been examined. Yet, rates of reaction are not conveniently predicted on the basis of either swelling or τ_c .³⁵ While JJ exhibits macroscopic swelling greater than MR, the rate of rotation of the radical in the swollen polymer is, in all cases, slower. This seems counterintuitive to conventional wisdom based on previous work on the relationship between swelling and τ_c .^{30,34} Reasons for this observation can be found in the mode of attachment of the radical probe. First, the formation of MR is fraught with variability. This is due to the different rates of reaction of divinyl benzene which is typically used as a mixture of *meta*- and *para*-isomers.³⁶ In addition, divinyl

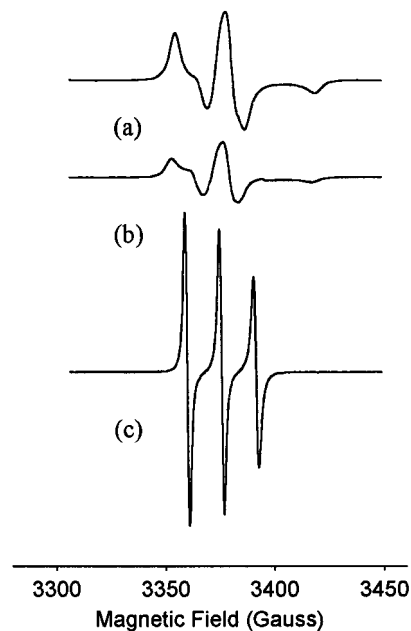


Figure 3. EPR spectra of radical labeled 2% cross-linked JandaJel (a) dry, (b) in EtOH, (c) in CH₂Cl₂.

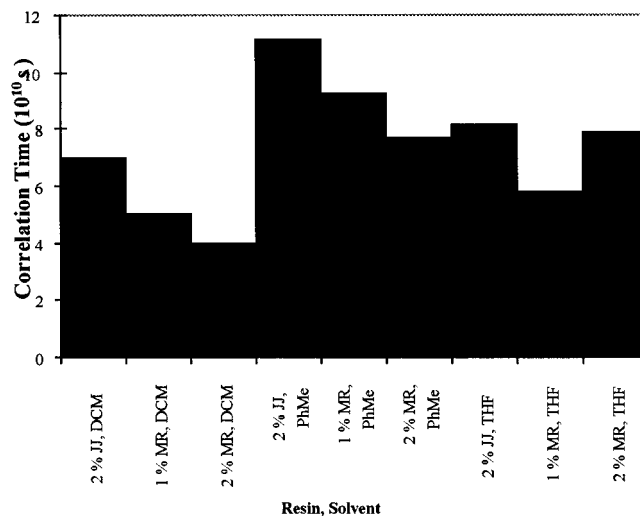


Figure 4. Correlation times for resins in different solvents.

benzene contains substantial quantities of ethylvinylbenzene. This combination of isomers and impurities gives rise to regions of greater and/or lesser cross-linking.³⁷ Second, as introduction of the nitroxide is only possible after polymerization, it potentially will not be uniformly distributed throughout the polymer. Third, as a tiny proportion of nitroxide is used, it will preferentially react at easily accessible sites. Hence, attachment of the probe occurs in regions of lower cross-linking. As such, conclusions drawn from EPR data should be considered valid only for a small portion of the resin, in other words, in regions where the nitroxide probe is attached. Finally, were each chloride substituted for a nitroxide a very different spectrum would result from excessive spin-spin coupling that would preclude observation of meaningful spectra.³⁵

Fluorescence Spectroscopy. A report examining the loading of gel-like supports through optical analysis of fluorescent probes bound to MR has recently appeared.³⁸ By attaching a rhodamine dye and examining slices of the

Table 1. Volume of Swollen Resins (mL/g)^a

resin (%CL)	Et ₂ O	PhMe	dioxane	EtOAc	THF	CH ₂ CL ₂	acetone	DMF
MR (2)	4.0	6.7	5.4	5.4	5.5	5.9	3.4	4.0
JJ (2)	5.2	9.7	8.2	8.0	8.3	7.8	4.4	5.4
MR (5)	3.4	4.7	5.1	4.3	4.7	5.4	3.4	3.7
JJ (5)	4.0	6.8	5.5	5.2	5.8	5.6	3.9	3.7
MR (10)	3.3	4.0	4.4	3.7	4.3	4.3	3.0	3.0
JJ (10)	3.5	5.9	5.6	4.2	5.5	5.5	3.1	3.1

^a Volumes were measured in syringes equipped with a sintered frit. The resin/solvent mixture was vortexed for 1 min to ensure intimate mixing and left to equilibrate for 1 h prior to volume measurement.^{49b} All resins had dry volumes of approximately 1.5 mL/g.

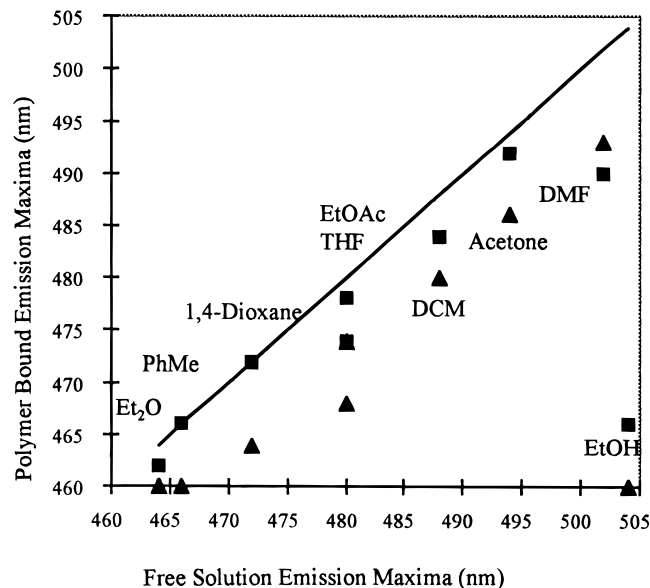


Figure 5. Emission maxima of free dansyl monomer vs emission maxima of dansyl monomer polymerized in a 2% cross-linked resin: \blacktriangle , MR; \blacksquare , JJ.

swollen beads with a laser, the authors reported that only sites on the surface of MR were functionalized, implying that swelling of the polymeric matrix plays only a small role in chemical reactivity. The above finding is in stark contrast to an earlier report,³⁹ in which a tritiated amino acid was attached to a cross-linked polystyrene bead. Slicing of the bead and examination of cross sections with an autoradiograph provided strong evidence of equally distributed radioactivity throughout the bead. Fluorescent data is useful because it unequivocally demonstrates interaction between solute and solvent, ruling out spurious results owing to differing porosities. Shifts in fluorescence maxima reveal the degree to which solvent molecules interact with the fluorescent probe on the polymer backbone. Dansyl probes are particularly useful for the study of microscopic interactions, as their fluorescence emission maximum is dependent upon their physicochemical microenvironment.⁴⁰ The emission maximum of the dansyl probe is highly dependent upon its solvation,⁴¹ therefore the fluorescence emission of the swollen polymer doped with such a probe will reflect the quality of the interaction between the solvent molecules and the probe itself. Information obtained in this way is instructive when compared with swelling data as it demonstrates the direct interaction between solvent molecules and the probe at the

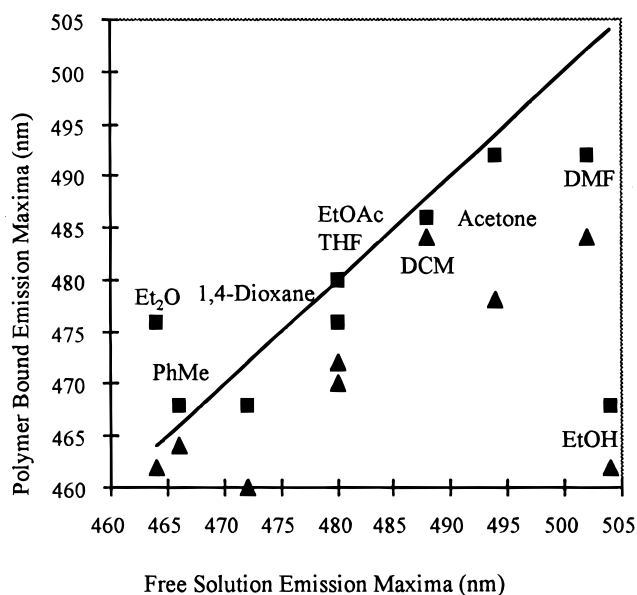


Figure 6. Emission maxima of free dansyl monomer vs emission maxima of dansyl monomer polymerized in a 5% cross-linked resin: \blacktriangle , MR; \blacksquare , JJ.

molecular level. Dansyl probes are, however, known to photobleach over long periods of time, and care must be taken to limit exposure to light.⁴²

N-Dansyl-4-vinylbenzylamine⁴³ was selected as the fluorescence probe. Emulsion polymerization of *N*-dansyl-4-vinylbenzylamine together with styrene and divinyl benzene (MR) or styrene and 1,4-bis(4-vinylphenoxy)butane (JJ) was performed to afford polymer beads having 2, 5, and 10% cross-linking, respectively.

The beads were pre-swollen in ethyl ether, toluene, 1,4-dioxane, ethyl acetate, THF, dichloromethane, acetone, ethanol, and DMF, respectively, prior to observation of the fluorescence spectrum. The swelling ability of the resins in these solvents is compiled in Table 1. Emission maxima of *N*-dansyl-4-vinylbenzylamine and the polymer-bound dansyl probe were then compared in a range of solvents (Figures 5–7 and Table 2). The closer the emission of the bound dye as compared to the line representing free solvation of the dansyl probe is an indication of better solvation, i.e., the probe experiences a microenvironment closely related to what it senses in free solution. Thus, that both dansylated polymers in EtOH should be far from the diagonal is to be expected as neither JJ nor MR swell in EtOH. The emission maxima for EtOH is in all cases near that obtained for the dry dansylated polymer. In keeping with previous results, as the degree of cross-linking increases, the emission maximum of the bound dye moves further from that of the unbound, consistent with a decreasing ability to achieve full solvation. In stark contrast to what was observed by EPR in all cases the JJ probe more closely approximates the solution phase. Even 5% cross-linked JJ more closely approximated free-solution behavior of the dansyl probe than did 2% MR in all but one solvent. Also, as the degree of cross-linking increases, with concomitant increase in mechanical stability, the difference in solvation between the JJ and the MR increases as well.

Many methods have been reported for determination of

Table 2. Comparison of Percent of Observed Fluorescent Maxima from Figures 5–8^a

	2% JJ ^b	2% MR ^b	2% JJ ^c	2% MR ^c	5% JJ	5% MR	10% JJ	10%MR
ethyl ether	99.6	99.1	101.5	101.7	102.6	99.6	99.6	98.3
PhMe	100.0	98.7	100.6	100.4	100.4	99.6	100.4	98.5
1,4-dioxane	100.0	98.3	100.6	100.8	99.2	97.5	98.7	97.0
THF	98.8	97.5	101.7	100.8	99.2	97.9	99.6	95.8
EtOAc	99.6	98.8	100.6	100.4	100.0	98.3	98.8	96.3
DCM	99.2	98.4	100.0	99.6	99.6	99.2	100.0	97.5
acetone	99.6	98.4	100.0	99.6	99.6	96.8	97.6	94.3
DMF	97.6	98.2	100.4	100.6	98.0	96.4	99.2	94.8
EtOH	92.5	91.3	93.5	94.0	92.9	91.7	92.5	90.5

^a Behavior of freely solvated probe is 100%. ^b Probe attached during polymerization. ^c Probe attached after polymerization.

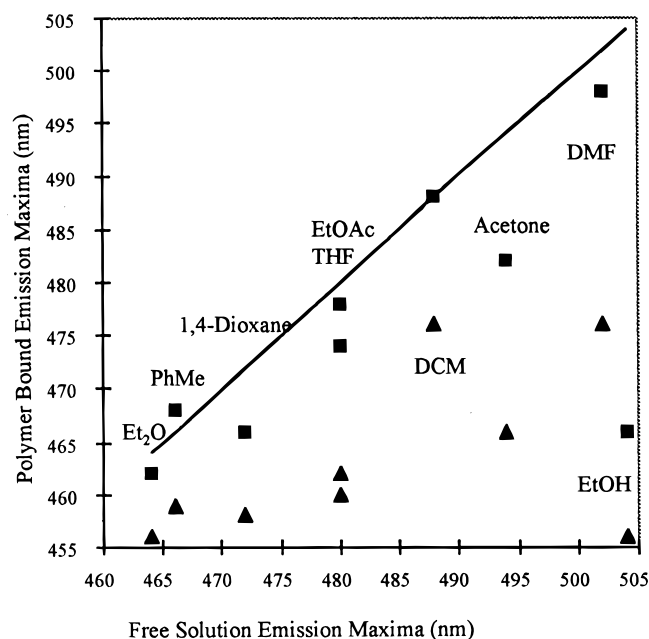


Figure 7. Emission maxima of free dansyl monomer vs emission maxima of dansyl monomer polymerized in a 10% cross-linked resin: ▲, MR; ■, JJ.

degree of swelling, for example, measurements of changes in volume for a single bead,⁴⁴ a syringe method,⁴⁵ and methods measuring changes in weight after centrifugation;⁴⁶ all of these methods are much more elaborate than simply measuring a change in volume. That the fluorescence data for the probe incorporated into the resin during polymerization corresponds well to the degree of swelling obtained by such relatively simple means⁶ reiterates the value of simply judging swelling by observation of changes in volume.

The dichotomy seen between the EPR and fluorescence experiments warranted further investigation between the two resins. Dansyl probes were attached to the chloromethyl groups of both 2% cross-linked MR and 2% cross-linked JJ after preformation of the bead. Owing to the sensitivity of the fluorescence spectrometer, only small amounts of the fluorescent material may be incorporated. A comparison of the emission maxima of the free probe and the probe attached to the resin after polymerization in a range of solvents is presented in Figure 8.

The most salient features between JJ and MR can be seen when comparing Figures 5 and 8. In most of the solvents examined, the emission maxima of the probe attached to JJ after polymerization more closely approximates the value

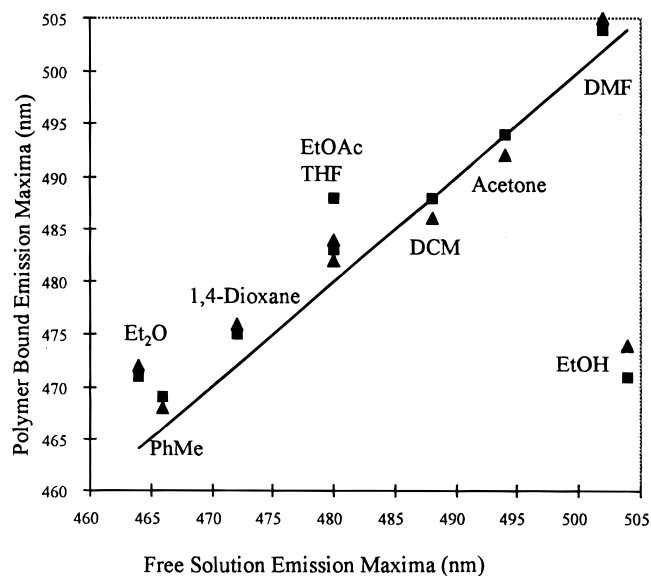


Figure 8. Emission maxima of free dansyl monomer vs emission maxima of dansyl monomer attached after polymerization to a 2% cross-linked resin: ▲, MR; ■, JJ.

of the free emission maxima probe, albeit this difference between the two resins is much smaller than that observed when the probe was incorporated as a monomer (Et₂O and EtOAc are similarly distant from the diagonal regardless of the means of attachment). Further contrast of Figures 5 and 8 provides evidence that the MR more closely mirrors the free dansyl probe only when the probe is attached after polymerization rather than when it is incorporated as a monomer. Again, we believe this latter finding may be the result of the formation of regions of high and low cross-link density. Such areas may arise during polymerization due to the inhomogeneity of the cross-linker used in the formation of MR (vide supra). Because this difference is less pronounced for JJ, we suggest that this resin provides a greater uniformity in morphology.

Conclusion

Two different physical methods have been employed for studying internal resin microenvironments. JJ is known to swell to a greater extent in most solvents commonly used by organic chemists than MR.⁶ Using fluorescence spectroscopy, a correlation between observed swelling and solvation effects on a fluorescent dansyl probe was observed. However, the internal viscosity, as determined by EPR spectroscopy, within JJ is higher than that within MR. Additionally the fluorescence spectroscopy technique was highly subject to

the method of incorporation of the probe into the resin. Taken as a whole, had only one of these physical techniques been used, the conclusions drawn would be very different. Consequently, we suggest that previous interpretations of a resin's microenvironment obtained from just EPR or fluorescence spectroscopy should be considered with caution, and that measurements on systems as complex as polymeric gels require probing of more than a single phenomena to ensure meaningful conclusions.

Experimental Section

General Methods. Fluorescence spectra were acquired on a SLM AMINCO SPF-500C spectrofluorometer. EPR spectra were recorded at room temperature on a Bruker EMX X-band spectrometer using a 4 mm quartz sample tube in a standard TE102 cavity. Spectra were collected at 9.52 GHz using 100 kHz field modulation of 1.0 Gauss, 1.0 mW microwave power. NMR spectra were recorded on a Bruker AMX 400 (^1H 400.134, ^{13}C 100.614 MHz). All materials, including Merrifield resin used in the attachment of the probes after polymerization, were used as received from Aldrich unless otherwise specified. Methanol was dried by distillation in the presence of $\text{Mg}(\text{OMe})_2$. The JandaJel used in the attachment of the probes after polymerization was synthesized as previously described.⁶ Styrene was washed with aqueous KOH, dried over MgSO_4 , and filtered immediately prior to use. *N*-Dansyl-4-vinylbenzylamine was prepared as previously described.⁴⁷

1,4-Bis(4-vinylphenoxy)butane. To a solution of 4-acetoxy styrene (50 mL, 0.32 mol) in MeOH (200 mL) was added a small piece of sodium metal. The mixture was left to stir overnight. Amberlite 120-IR (H^+) was added, and stirring was continued for 30 min. The resin was removed by filtration, and the solvent was removed under reduced pressure to afford a white solid, which was not isolated. The solid was dissolved in DMF (150 mL), and NaH (60% dispersion in mineral oil, 16 g, 0.4 mol) was added in portions. The mixture was heated at 85 °C for 1 h. 1,4-Dibromobutane (21.5 mL, 0.18 mmol) in DMF (50 mL) was added dropwise over the course of an hour. The mixture was left to stir overnight. The mixture was poured into ice water (500 mL), filtered, and recrystallized from PhMe to afford the product as a white solid (40.2 g, 85%). mp: 126–127 °C (lit⁴⁸ 127–128.5 °C). ^1H NMR (400 MHz, CDCl_3): δ 2.02 (s, 2 H, CH_2), 4.05 (s, 2 H, CH_2), 5.17 (d, 1 H, J 12.5 Hz, $\text{CH}=\text{CH}_2$), 5.63 (d, 1 H, J 12.5 Hz, $\text{CH}=\text{CH}_2'$), 6.62 (m, 1 H, $\text{CH}=\text{CH}_2$), 6.87 (d, 2 H, J 3.4 Hz, $\text{H}_{\text{Ph}}-2,6$), 7.37 (d, 2 H, J 3.5 Hz, $\text{H}_{\text{Ph}}-3,5$). ^{13}C NMR (100 MHz, CDCl_3): δ 25.99 (CH_2), 67.45 (CH_2), 111.53 ($\text{C}=\text{CH}_2$), 114.47 ($\text{C}=\text{CH}_2$), 127.39, 130.36, 136.23, 158.77 (Ph).

Synthesis of Fluorescent Resins. (a) Incorporation during Polymerization. Argon was bubbled through a solution of acacia gum (5.4 g) and NaCl (3.4 g) in water (135 mL) as the temperature was raised to 85 °C over 1 h. A solution of styrene (7.05 mL, 61.5 mmol), benzoyl peroxide (135 mg), *N*-dansyl-4-vinylbenzylamine (4 mg, 10.9 μmol), and cross-linker (divinyl benzene [80%]: 0.22 mL [1.23 mmol]; 0.55 mL [3.1 mmol]; 1.1 mL [6.1 mmol], 1,4-bis(4-vinylphenoxy)butane: 361 mg [1.23 mmol]; 904 mg

[3.1 mmol]; 1.81 g [6.1 mmol]) in chlorobenzene was subjected to argon bubbling. The organic solution was added to the stirred aqueous solution. Stirring was accomplished using a floating magnetic stirrer in a 200 mL three-necked reaction flask.⁴⁹ Stirring at 85 °C was continued for 20 h. The solid was isolated by filtration, washed with copious water, and extracted with acetone in a Soxhlet extractor for 6 h prior to vacuum-drying at 50 °C under reduced pressure.

(b) Incorporation after Polymerization. A mixture of dansylamine (0.07 mg, 2.8 μmol) and NaH (60% dispersion in mineral oil, 3 mg, 7.5 μmol) was heated at 80 °C for 1 h in DMF (2 mL). The mixture was added to a mixture of resin (2 g) that had been preswollen 1 h in DMF, and the mixture was stirred at 80 °C for 20 h. The solid was isolated by filtration, washed with copious amounts of aqueous dioxane, DMF, acetone, and CH_2Cl_2 , and was dried under reduced pressure.

Nitroxide Spin Label Attachment. Resin [(1 g) chloromethylated 2% Merrifield resin, 1% Merrifield resin, 2% JandaJel] was swollen in DMF (20 mL) that previously had argon bubbled through it for an hour. To 2,2,6,6-tetramethyl-4-piperidinol-1-oxy (5.1 mg, 29.5 μmol) in DMF (8 mL) was added NaH (100 mg, 2.5 mmol), and the mixture was left to stir 1 h. An aliquot of the radical solution (2.5 mL) was added to each of the swollen resins, and the mixture was left to stir overnight. The solids were collected by filtration and washed sequentially with copious water, EtOH, PhMe, and Et_2O . The resins were dried under reduced pressure.

Fluorescence Experiments. The resins (250 mg) were allowed to equilibrate with solvent (2.5 mL) for 1 h⁵⁰ prior to observation of the fluorescence emission spectra in a 1 cm \times 1 cm quartz cuvette. Excitation was achieved at 380 nm.

EPR Experiments. The resins were allowed to equilibrate with solvent in a sealed EPR tube for 1 h⁵⁰ prior to acquisition of the spectra. All solvents were subjected to three freeze–thaw cycles immediately prior to use, and all manipulations were carried out under a blanket of argon.

Density Measurements. A known amount of resin was added to a graduated cylinder containing hexane (2 mL). The mixture was thoroughly shaken and left to equilibrate for 1 h. The change in volume was noted. For 2% cross-linked Merrifield resin $\rho = 1.206$ g/mL, and for 2% cross-linked JandaJel $\rho = 1.092$ g/mL. Hexane was used as it has been demonstrated not to interact with the resin⁴⁴ and has a substantially lower surface tension than other noninteracting solvents.

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