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High-Resolution Diffusion-Ordered Spectroscopy To Probe the Microenvironment of *J*anda*J*el and Merrifield Resins

Céline Gambs, Tobin J. Dickerson, Suresh Mahajan, Laura B. Pasternack, and Kim D. Janda*

Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037

kdjanda@scripps.edu

Received February 3, 2003

The success of organic reactions performed on a gel-phase resin is highly dependent on the accessibility of solvents, catalysts, and reagents to the interior of the resin. A variety of techniques including EPR, fluorescence, and Hildebrand solubility parameters (δ) have been used to probe reaction capabilities and in particular the microenvironment of a gel-phase resin. To provide a more detailed picture of the matrix in question, researchers have turned to NMR for the determination of the diffusion coefficients of solvents and small molecules in swollen beads to provide a means to compare the microenvironment of swollen beads. Since Merrifield and *J*anda*J*el resins display different swelling properties and have significantly different kinetic behavior, we undertook a comparative study of the diffusion coefficients of solvents and small molecules in both resins by high-resolution ^{1}H DOSY NMR. Our results show the following: (1) diffusion values for all studied solvents and small molecules are 20−30% higher in *J*anda*J*el compared to Merrifield resins, (2) in the absence of interactions between the resin and a given molecule, the diffusion values mirror the swelling properties of the resin, and (3) in the presence of strong intermolecular interactions between the gel and the considered molecule, the diffusion behavior in the gel is primarily influenced by the strength of the interactions and secondarily by the swelling properties of the resin. These results clearly show that the microenvironment of *J*anda*J*els is more “solution-like” than that of Merrifield resins, presumably due to the higher swelling capacity.

Introduction

Solid-phase organic synthesis (SPOS) has become a powerful methodology for the generation of compound libraries.[1] However, the success of this technique is highly dependent on the accessibility of the functional sites of the polymer to reagents. Concurrent with the resurgence in solid-phase synthesis has been the recognition that chemical reactivity of a supported small molecule, catalyst, or reagent may be significantly altered by so-called “polymer effects”, the origins of which may be physical or chemical. Thus, it is no longer reasonable to depict the polymer matrix as a simple ball or to consider the support as a rigid inert material. The support interacts with the surrounding medium and can impact the kinetics of the reaction, clearly implicating it as more than a simple bystander. As such, in developing synthetic routes to molecules on a gel-phase support, one must consider not only the functional group distribution along the polymer chain but also the three-dimensional arrangement of the anchored functional groups. Additionally, the nature of the polymer backbone must also be considered as the composition of the support can have a pronounced impact on the success of a chemical synthesis.

Styrene-based polymers remain the most widely used supports in SPOS.[2] Mainly, this is due to their ready availability and proven use in the field of Merrifield polypeptide synthesis. Additionally, the development of new resins that are economically viable, exhibit satisfactory physical characteristics, and are inert to a diverse range of reagents or catalysts is a significant undertaking, and as such, Merrifield resins have remained the gold standard for SPOS. However, it has been recognized that while tailoring new gel-based resins is nontrivial, new resins will be needed if the field of SPOS continues to grow. Strategies to identify polymeric supports that are more suitable for SPOS have included the reformatting of the divinylbenzene polystyrene resins (DVB-PS);[3] the addition of either poly(ethylene glycol) (PEG),[4] poly-

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* Corresponding author. Phone: 858-784-2516. Fax: 858-784-2595.

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10.1021/jo034152z CCC: \$25.00

styrene,[5] or hydrocarbon[6] grafts to DVB-PS resins; the use of macroporous polystyrene-[7] or PEG[8]-based matrixes; and the grafting of polystyrene onto polypropylene[9] or Teflon surfaces.[10]

A different approach that has recently emerged involves the replacement of divinylbenzene (DVB) as the cross-linker in polystyrene resins with a more flexible molecule. Recently, we introduced resins based on flexible polytetrahydrofuran (PTHF) cross-linkers, termed *J*anda*J*els.[11] Our efforts using this resin type have revealed several significant advantages to these supports, including the ease of preparation of a highly pure cross-linker, which translates into a more homogeneous resin and improved chemical stability relative to flexible cross-linker counterparts containing PEG.

Since our initial disclosure of *J*anda*J*el resins, there has been increasing application of this type of resin in SPOS in the construction of small molecule libraries.[12] In addition, *J*anda*J*els have been applied successfully as the support for catalysts in enantioselective epoxidation,[11b] Strecker,[13] Reissert-type,[14] and asymmetric allylic substitution[15] reactions. In comparative experiments, *J*anda*J*el-supported catalysts have been reported to promote reactions in higher yields and increased enantioselectivities over Merrifield-supported catalysts. These results suggest that the higher swelling characteristics of *J*anda*J*el allow for better solvation and render the polymer-supported catalyst more accessible, giving comparable results to those obtained with the homogeneous systems.[13] Additionally, the increased swelling capacity of *J*anda*J*el allows the solid-phase preparation of the classic difficult peptide sequence ACP(65−74) in significantly higher purity than when employing a corresponding Merrifield resin.[11c]

To date, a series of methods have been applied to compare and contrast the microenvironments and dynamics of *J*anda*J*el and Merrifield resins. The Flory−Rehner theory[16] was applied to estimate the swelling ability of *J*anda*J*el and Merrifield resins by comparing the differences in Hildebrand solubility parameters (δ)[17] between polymer and solvent. These results indicated that Merrifield resins should have better swelling properties than *J*anda*J*el in most organic solvents,[18] in contradiction to experimental observations.[11a] To explore this disparity, EPR and fluorescence spectroscopy also have been used to study the internal microenvironment of the two resins.[18] Studies with EPR spectroscopy showed that the internal viscosity within swollen *J*anda*J*els was higher than that within Merrifield resins; however, these results contradicted previous studies on the relationship between swelling and correlation time (τ_c).[19] Data obtained with fluorescence spectroscopy on swollen polymer doped with a dansyl probe provided the expected correlation between observed swelling and solvation effects. In light of this, we have become interested in closely examining this dichotomy observed in the previously obtained physical measurements and have undertaken a study to compare the diffusion of solvents and small molecules in *J*anda*J*el and Merrifield polymer matrixes.

Several methods for elucidating the diffusion behavior of solvents in gels are available. Since the development of the pulsed field gradient (PFG) NMR techniques in 1965,[20] this approach has found wide application in studies of diffusion of organic substances in a diverse set of materials. By employing matched gradient pulses to encode information about the translational motion of a sample, direct measurements of the diffusion of small molecules can be made. For example, extensive studies into the diffusion of solvents and small molecules in polystyrene gels have been reported with use of pulsed gradient spin−echo (PGSE) and magnetization transfer (MT) NMR methods.[21] In fact, these elegant studies have demonstrated that the diffusion rates of toluene in cross-linked and non-cross-linked polystyrene gels at similar concentrations were remarkably similar. These results further suggested that the diffusion rate in cross-linked polymer beads was not significantly affected by the presence of cross-links, but mainly determined by the concentration of solvent in the bead.[21a]

Various NMR techniques have been applied to investigate the structure and the dynamics of several polymer gel systems.[22] For example, ^{1}H NMR imaging has been used to provide spatial information about the diffusion

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TABLE 1. Measured Diffusion Coefficients (D, $\times 10^{-10}$ m^2 s^{-1}) for Solvents

	self-diffusion	J-NH$_2$	J-OH	M-NH$_2$	M-OH
THF	30.5 ± 3.3	24.8 ± 0.3	17.8 ± 0.02	17.8 ± 0.2	14.0 ± 0.1
DMF	17.8 ± 0.4	10.6 ± 0.2	9.1 ± 0.1	8.1 ± 0.04	6.8 ± 0.001
Toluene	30.4 ± 1.2	14.7 ± 0.1	11.9 ± 0.2	12.1 ± 0.2	7.3 ± 0.1

process of molecules in gels.[23] Recently, pulsed field gradient spin−echo (PFGSE) NMR has been applied to elucidate the diffusion behavior of soluble polymers, solvents such as THF and DMF, and amino acids in polymer gel systems, including Merrifield resins and polyacrylamide.[24] The contemporary technology of PFGSE can also be extended into a multidimensional format and the experiment, termed diffusion ordered spectroscopy (DOSY), results in a pseudo-two-dimensional data set with diffusion coefficients displayed along one axis and the chemical shifts on the other.[25] Equipment for DOSY experiments now have automated data collection with a programmed set of gradient amplitudes, rendering the execution of these experiments very straightforward compared to previous methodologies. Additionally, diffusion NMR-based methods such as DOSY benefit from a key advantage over other techniques such as EPR and fluorescence. Compounds to be analyzed can be used directly in standard solvents without chemical modification, allowing real-time diffusion measurements to be rapidly obtained without prior adjustment of the reaction system.

In this study, we have attempted to garner a deeper understanding of diffusion processes in functionalized *J*anda*J*el and Merrifield resins using DOSY. A better appreciation of the factors that influence the diffusion rate of solvents and reagents in these polymer networks is of great importance, particularly for solid-phase organic reactions that are kinetically controlled and in the development of improved resin matrixes for SPOS.

Results and Discussion

The diffusion coefficients (D) of solvents and small molecules in solution and swollen aminomethyl and hydroxymethyl *J*anda*J*el and Merrifield resin beads were determined at 30 °C by high-resolution ^{1}H DOSY NMR with gradient pulse amplitudes ranging from 5 to 25 G cm^{-1}.

Diffusion of Solvents in *J*anda*J*el and Merrifield Resins. The diffusion coefficients (D) of DMF, THF, and toluene in solution (D_0^{solvent}) and in four different resins ($D_{\text{resin}}^{\text{solvent}}$; *J*anda*J*el-NH$_2$, *J*anda*J*el-OH, Merrifield-NH$_2$, and Merrifield-OH) were measured by using the standard "one-shot" pulse sequence provided by Varian, Inc. (Table 1).[26] Gratifyingly, the self-diffusion coefficients for THF and DMF were found to be very close to previously reported values,[24f] confirming the reliability of the employed DOSY pulse sequence.[27]

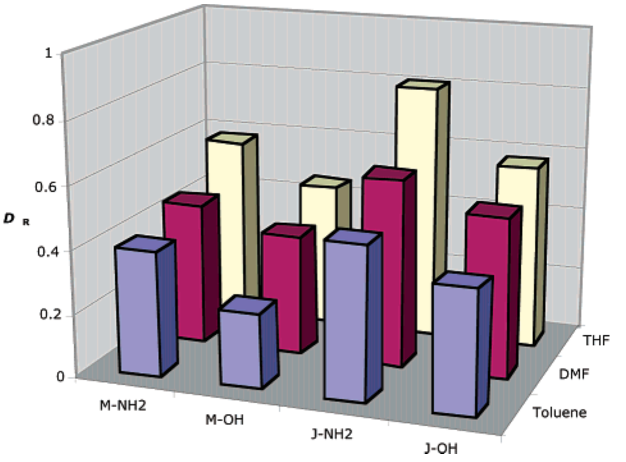

FIGURE 1. Reduced self-diffusion coefficients (D_R) of toluene, DMF, and THF.

To gain a better understanding of the microenvironment of the swollen resin as it relates to the solution behavior, it is necessary to compare the diffusion coefficients in solution to the diffusion coefficients in the swollen resins. Therefore, we define a reduced diffusion coefficient D_R as the ratio of the diffusion coefficient of the solvent in a swollen resin to the self-diffusion coefficient of the solvent ($D_R = D_{\text{resin}}{}^{\text{solvent}}/D_0{}^{\text{solvent}}$).[24f] In solution, the reduced diffusion coefficient is, by definition, equal to 1. Thus D_R values close to 1 indicate a resin microenvironment that closely resembles solution conditions, and conversely, values of D_R close to 0 imply a resin microenvironment with no solution characteristics, potentially attributable to a number of factors including resin−solvent interactions and the limited porosity of the resin. Intermediate values of D_R provide numerical values indicating deviation from solution behavior as it relates to diffusion, and as such, allow a quantitative comparison between different resins.

The data for solvent diffusion (Table 1) were converted to reduced diffusion coefficients and compared as a function of the resin (Figure 1). Several key observations can be made from these data including the following: (1) The reduced diffusion coefficients are 20−30% higher for *J*anda*J*els as compared to Merrifield resins, (2) the reduced diffusion coefficients decrease in the order of THF > DMF > toluene for all resins studied, and (3) the

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(26) A complete description of the resins used is found in the Experimental Section.

(27) See Supporting Information for statistical analysis of the DOSY and polymer swelling data.

TABLE 2. Measured Diffusion Coefficients for Small Molecules, (D, $\times 10^{-10}$ m^2 sec^{-1})

molecule examined	solvent	solution	JJ-NH$_2$	JJ-OH	M-NH$_2$	M-OH
Boc-glycine	DMF-d_7	8.0 ± 0.3	1.6 ± 0.01	3.2 ± 0.1	1.0 ± 0.03	2.0 ± 0.04
Boc-glycine methyl ester	DMF-d_7	9.8 ± 0.1	4.2 ± 0.001	3.6 ± 0.1	3.9 ± 0.1	2.5 ± 0.1
p-xylene	DMF-d_7	14.8 ± 0.2	6.9 ± 0.4	5.8 ± 0.3	5.7 ± 0.4	3.8 ± 0.2
p-xylene	toluene-d_8	31.7 ± 0.04	9.2 ± 0.4	8.0 ± 0.2	7.9 ± 0.3	5.4 ± 0.2

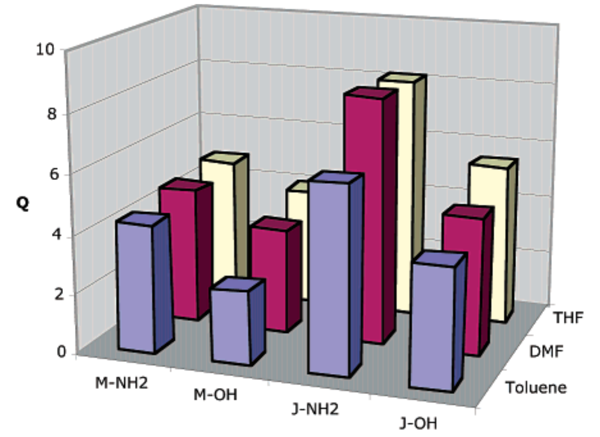

FIGURE 2. Swelling ratio (Q) of resins in DMF, THF, and toluene.

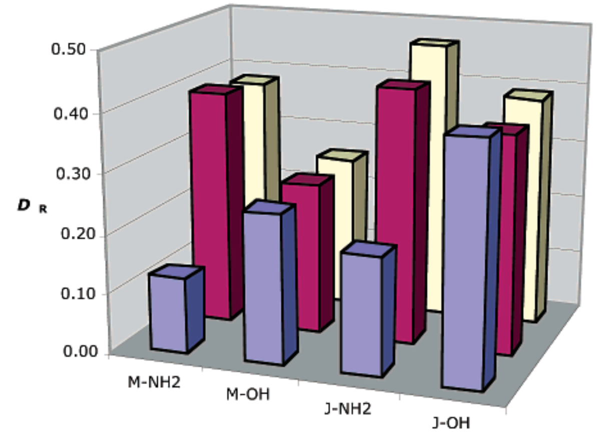

FIGURE 3. Reduced diffusion coefficients (D_R) of Boc-glycine (blue), Boc-glycine methyl ester (maroon), and *p*-xylene (yellow) solutions in DMF-d_7.

reduced diffusion coefficients are significantly higher for resins with aminomethyl functionality as compared to resins with hydroxymethyl functionality. It is well-known that *J*anda*J*els have significantly higher swelling volumes compared to Merrifield resins.[11] Solvents and cross-linkers play a key role in determining the swelling of the resin. Thus the higher reduced coefficients observed for *J*anda*J*els must be due to the more flexible and polar cross-linker leading to increased swelling. We also propose that the higher diffusion coefficients observed for THF as compared to DMF and toluene, and in the case of aminomethyl versus hydroxymethyl based resins, can also be explained by the swelling characteristics of the resins.

To confirm our hypothesis, we determined the swelling ratio, Q,[24f] for each resin in the same panel of solvents.[27] This ratio is defined as the ratio of the volume of the swollen resin to the volume of dried resin. In agreement with our NMR diffusion data, *J*anda*J*el-NH$_2$ possesses excellent swelling properties in the three organic solvents, and the swelling ratio is significantly higher than that measured for Merrifield-NH$_2$; similar observations can be made by comparing *J*anda*J*el-OH to Merrifield-OH (Figure 2).

These results confirm that the incorporation of the PTHF cross-linker in *J*anda*J*el resins grants greater swelling of the polymer network in common organic solvents. It is important to note the diffusion behavior (Figure 1) closely mirrors the observed swelling volume trends (Figure 2). Thus, the three noted observations regarding the diffusion behavior in *J*anda*J*el versus Merrifield resins, THF versus DMF and toluene, and aminomethyl versus hydroxymethyl functionality can be explained to a first approximation by the higher swelling of *J*anda*J*el relative to the corresponding Merrifield resin. Ando and co-workers recently reported that the reduced diffusion coefficients of DMF and THF in chloromethyl-functionalized Merrifield resins exhibit a linear correlation with the swelling ratio, and are independent of the solvent when no strong intermolecular interactions occur between the solvent molecules and polymer network.[24f] In our studies, we did not find a true linear correlation between D_R and the swelling ratio; however, the majority of our data is comparable to the linear behavior observed by Ando. In conjunction with Ando's data, our data imply a strong relationship between the swelling volumes and the diffusion of solvents within swollen resins. Other factors, such as cross-linkers and pendant functional groups, may play a minor role in the diffusion behavior of the solvents; however, our findings clearly indicate the major determinant in the diffusion behavior is the swelling volume.

Diffusion of Boc-glycine and Boc-glycine Methyl Ester in *J*anda*J*el and Merrifield Resins. Although the diffusion behavior of solvents in gels provides insight about the microenvironment of the resins, the performance of these resins in SPOS requires an understanding of the diffusion behavior of molecules relevant to the practice of organic synthesis. Therefore, we determined the diffusion behavior of 5 wt % solutions of three small molecules, Boc-glycine, Boc-glycine methyl ester, and *p*-xylene in Merrifield resins and *J*anda*J*els in DMF-d_7 using high-resolution ^{1}H DOSY NMR (Table 2).

Interestingly, the reduced diffusion coefficients for Boc-glycine in hydroxymethyl functionalized *J*anda*J*el and Merrifield resins are approximately 50% higher than those of their corresponding aminomethyl functionalized resins (Figure 3). Given the swelling properties of the four resins in DMF (Figure 2), one may have predicted the highest diffusion coefficient would have been obtained in *J*anda*J*el-NH$_2$, which displays the highest swelling ability in DMF. However, considering the low reduced diffusion values obtained in the presence of both aminomethyl functionalized resins, one can infer that an ion-pair forms between the free carboxylic acid of Boc-glycine and the primary amino group of the resin. In essence, this behavior is identical to an ion-exchange resin. To confirm this assumption, we determined the diffusion behavior of Boc-glycine methyl ester. Both Boc-glycine and Boc-glycine methyl ester have very similar molecular sizes; however, Boc-glycine methyl ester cannot form an ion-pair with the functionalized resins. Gratifyingly, our results strongly support our hypothesis that functional group interactions are primarily responsible for the surprising results with Boc-glycine, as with Boc-glycine methyl ester, the diffusion values follow the expected trend. The reduced diffusion coefficients for Boc-glycine methyl ester decrease in the order $D_{\mathrm{JJ-NH2}}^{\mathrm{Boc-Gly-OMe}} > D_{\mathrm{M-NH2}}^{\mathrm{Boc-Gly-OMe}} \approx D_{\mathrm{JJ-OH}}^{\mathrm{Boc-Gly-OMe}} > D_{\mathrm{M-OH}}^{\mathrm{Boc-Gly-OMe}}$ and the swelling abilities of the resins decrease in the same order $Q_{\mathrm{JJ-NH2}}^{\mathrm{Boc-Gly-OMe}} > Q_{\mathrm{M-NH2}}^{\mathrm{Boc-Gly-OMe}} \approx Q_{\mathrm{JJ-OH}}^{\mathrm{Boc-Gly-OMe}} > Q_{\mathrm{M-OH}}^{\mathrm{Boc-Gly-OMe}}$.

These experiments have clearly demonstrated that the diffusion coefficients of Boc-glycine and Boc-glycine methyl ester molecules are much higher in *J*anda*J*els than in Merrifield resins, suggesting that the microenvironment created in swollen *J*anda*J*els is more favorable for the mobility of small molecules. In addition, we have presented compelling evidence that in the presence of strong ion-pair interactions between aminomethyl functionalized matrixes and Boc-glycine, the molecular mobility of Boc-glycine decreases drastically and the internal viscosity is expected to increase. By contrast, in the absence of strong interactions as is the case between Boc-glycine methyl ester and the polymer support, the diffusion values of the protected amino acid in all studied resins increase with a concomitant increase in the degree of swelling (Q) of the polymer network.

Interestingly, the data also clearly show that reduced diffusion coefficients for both *p*-xylene and Boc-glycine methyl ester are very similar, indicating that the approximately 2-fold change in hydrodynamic volume between the two compounds is not significant relative to the pore size of the resins. As in the case of the Boc-glycine methyl ester, *p*-xylene is expected to have minimal interactions with pendant functional groups and therefore the D_R values closely mirror the swelling volume behavior of the resins (Figure 3).

Diffusional behavior of *p*-Xylene in DMF and Toluene. To investigate the role solvent interactions with a small molecule can play in determining D_R, the diffusion of *p*-xylene was also studied in toluene-d_8 (Table 2). The reduced diffusion coefficients (D_R) of the 5% *p*-xylene solution in both DMF-d_7 and in toluene-d_8 are significantly higher in *J*anda*J*el resins compared to Merrifield analogues as clearly indicated in Figure 4. Consistent with our hypothesis, it is noteworthy the D_R values of the 5% *p*-xylene solution in both DMF-d_7 and toluene-d_8 increase with Q. Moreover, it is interesting to note that even in the complete hydrophobic medium of toluene, the diffusion of *p*-xylene is favored in *J*anda*J*el relative to Merrifield resins, despite the presence of a polar cross-linker in *J*anda*J*el. In all cases, the diffusion coefficient in toluene is approximately 65% of the diffusion coefficient in DMF, suggesting that the predominant factor in determining the diffusion of *p*-xylene in a gel-type polystyrene-based resin is simply the swelling capacity of the resin and that solvent−*p*-xylene interactions play no significant role.

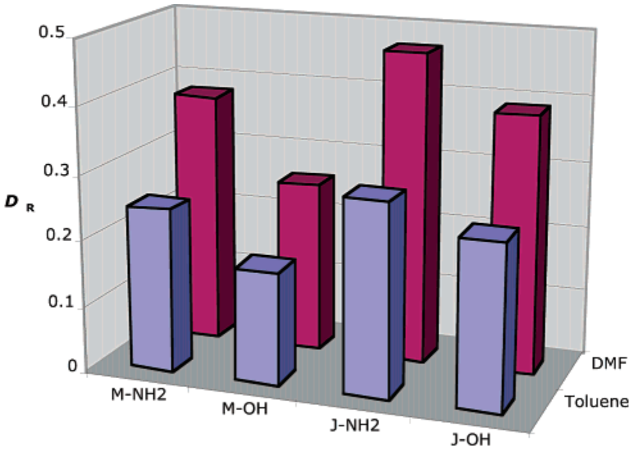

FIGURE 4. Reduced diffusion coefficients (D_R) of 5% *p*-xylene solution in DMF-d_7 and toluene-d_8 for all resins studied.

Conclusion

The compilation of our data has clearly demonstrated a connection between a macroscopic observable, resin-swelling capacity, with a molecular phenomenon critical to chemical reactivity, diffusion. Reduced diffusion coefficients of solvents (DMF, THF, toluene) and small molecules (Boc-glycine methyl ester, *p*-xylene) are 20−30% higher in *J*anda*J*el than in Merrifield resins, clearly indicating a microenvironment that more closely resembles solution behavior. Our experimental results suggest that in the absence of strong interactions between the resin and the solvents or the small molecules, the swelling properties of the resin significantly influence the diffusion values. In contrast, we have also shown that in the presence of strong intermolecular interactions between the resin and dissolved molecules such as with Boc-glycine and aminomethyl-functionalized matrixes, a drastic decrease of the diffusion values is observed, potentially having a marked effect on chemical reactivity. In this case, the diffusion behavior in the gel is primarily influenced by the strength of the intermolecular interactions and secondarily by the swelling properties of the resin. Despite the wide use of Merrifield resins and the continued use of our *J*anda*J*el supports in solid-phase organic synthesis (SPOS), very few kinetics studies have been reported thus far.[18b,28] Consequently, comprehensive investigations are underway in our laboratory to conclusively link the effects of the increased swelling of *J*anda*J*el and chemical reactivity and our results will be reported in due course.

Experimental Section

Resin Description. Each of the resins (100−200 mesh) used in these experiments was purchased from commercial sources. The loading levels of each resin were the following: *J*anda*J*el-NH$_2$, 1.30 mmol/g; *J*anda*J*el-OH, 1.34 mmol/g; Merrifield-NH$_2$, 1.30 mmol/g; and Merrifield-OH, 1.46 mmol/g. No correction was made based on loading in any of the described experiments.

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(28) (a) Gerritz, S. W.; Trump, R. P.; Zuercher, W. J. *J. Am. Chem. Soc.* **2000**, *122*, 6357−6363. (b) Li, W.; Xiao, X.; Czarnik, A. W. *J. Comb. Chem.* **1999**, *1*, 127−129. (c) Li, W.; Czarnik, A. W.; Lillig, J.; Xiao, X.-Y. *J. Comb. Chem.* **2000**, *2*, 224−227. (d) Merrifield, B. *Br. Polym. J.* **1984**, *16*, 173−178.

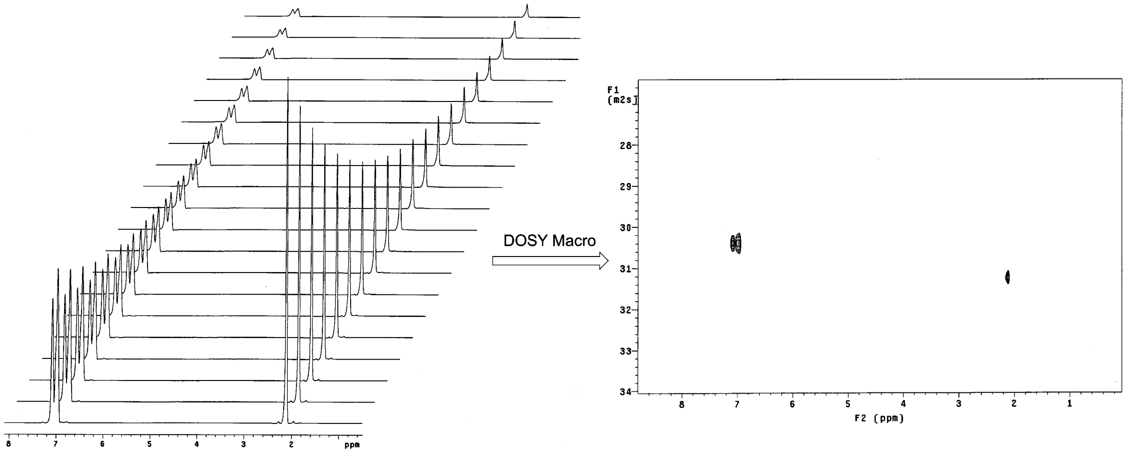

FIGURE 5. Sample ^{1}H NMR and DOSY spectra.

Swelling Volume Determination. The swelling volume of the resins was determined by previously published methods.[11a] Briefly, 50 mg of the appropriate dry resin was added to a 1-mL syringe equipped with a polyethylene filter. The appropriate solvent was then added and the mixture vortexed for 30 s for maximum resin/solvent mixing. The resin was allowed to stand for 1 h for equilibration, and the volume of swollen beads was recorded. The swelling ratio of the resin (Q) is defined as the ratio of the volume of a swollen resin at room temperature (V_{swollen}) to the volume of dry resin (V_{dry}). The swelling ratios determined are the average of a minimum of 3 replicates of each resin.

NMR Spectroscopy. The diffusion coefficient measurements were carried out at 30.0 ± 0.1 °C by performing HR-DOSY-NMR experiments, using a 400-MHz actively shielded spectrometer equipped with a gradient pulse amplifier and a 5-mm probe capable of producing up to 30 G cm^{-1} z field gradient pulses. The diffusion measurements were made by using the one-shot pulse sequence. The pulse and spectra width were adjusted to 6.8 ms and 6395.9 Hz, respectively. The free induction decay contained 32 000 data points. For all the experiments, 15−20 spectra (8−16 transients each) were collected with gradient pulse amplitudes ranging from 5 to 25 G cm^{-1}, where an approximately 90−95% decrease in the resonance intensity was achieved at the largest gradient amplitudes. The baselines of all arrayed spectra were corrected prior to processing the data. After data acquisition, each FID was apodized with line broadening of 1.0 (for solution) and 10.0 Hz (for gels), and Fourier transformed. A DOSY macro then determines the peak heights of all the signals above a preestablished threshold and fits the decay curve for each peak to a Gaussian function. The DOSY macro was run with data transformed by using fn = 100 000. The results of the DOSY method of analysis are pseudo-two-dimensional spectra with NMR chemical shifts along one axis and calculated diffusion coefficients on the other axis. A sample of the raw ^{1}H NMR data and DOSY spectra can be found in Figure 5.

All samples for NMR analysis were prepared in 5-mm tubes by adding the appropriate resin (100−250 mg) to the tube followed by excess solvent (DMF, THF, toluene) or solution (5 wt % DMF-d_7 solution of Boc-glycine, Boc-glycine methyl ester, *p*-xylene, or a 5 wt % *p*-xylene in toluene-d_8) to fully swell the resin. The amount of resin used for each experiment was not critical, provided that the swollen resin occupied the entire active sample volume, and no free solvent was present within this space. The samples were allowed to equilibrate for at least 2 days to achieve uniform solvent/solution uptake. Air bubbles were removed from the sample by vortexing. The samples were allowed to equilibrate for another 2 h and the excess solvent/solution was removed from the tube prior to NMR data acquisition. All reported diffusion coefficient values are the average of a minimum of three replicates.

Acknowledgment. This work was supported financially by The Scripps Research Institute, The Skaggs Institute for Chemical Biology, the National Institutes of Health (GM-56164 to K.D.J.; DA-15973 to T.J.D.), and the Swiss National Foundation and Novartis Foundation (postdoctoral fellowship to C.G.). We thank Dr. Anita D. Wentworth for helpful discussions.

Supporting Information Available: Statistical analysis of diffusion coefficient, D_{R}, and swelling ratio determination. This material is available free of charge via the Internet at http://pubs.acs.org.

JO034152Z