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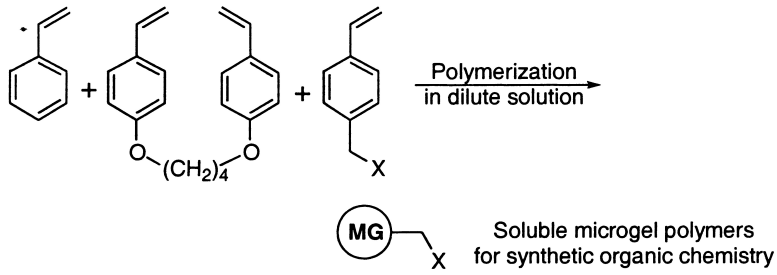

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Application of Microgels as Polymer Supports for Organic Synthesis: Preparation of a Small Phthalide Library, a Scavenger, and a Borohydride Reagent

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Microgel polymers containing a series of functional groups have been prepared. These microgels were composed of cross-linked poly(styrene) and were prepared by radical polymerization in solution. The microgel polymers exhibit good solubility in an array of different organic solvents, and in addition, they can be efficiently precipitated by the addition of methanol and isolated by filtration. A nine-member phthalide library was synthesized using an aminomethyl-functionalized microgel **5**. To further demonstrate the versatility of these microgel polymers, tris(2-aminoethyl)amino microgel **11** was examined as a scavenger reagent to remove unreacted isocyanate after a urea synthesis. Finally, a microgel-supported ammonium borohydride reagent **14** was successfully prepared and used as a reducing agent. Notable features of these microgels are that in all applications the progress of the reaction could be monitored by standard NMR techniques and their preparation is performed using common glassware and techniques found in all organic laboratories.

Introduction

The most commonly used methodology for construction of libraries of small molecules is solid-phase organic synthesis (SPOS).[1] In SPOS, support-bound substrates are elaborated by using excess reagents to drive reactions to completion. SPOS has many advantages but also has drawbacks; for example, it can be difficult to adapt conventional solution-phase chemistry to the solid-phase format. In addition, the progress of solid-phase reactions can be difficult to monitor. Linear soluble polymers such as poly(ethylene glycol) (PEG) and non-cross-linked poly(styrene) have been used in liquid-phase organic synthesis (LPOS)[2] to obviate some of the drawbacks found in SPOS. Soluble polymers can be added to a poor solvent that causes the polymer to precipitate, which enables isolation by filtration. PEG-based soluble polymers have low solubility in THF,[3] ethyl acetate, and acetone, and they tend to precipitate at low temperatures. In addition, PEG is not stable to strong acids or to some organometallic reagents. Linear polystyrene has good solubility characteristics, but at high concentrations and low temperatures the solution becomes extremely viscous.

Microgels offer an attractive alternative to linear soluble polymers. This interesting class of materials is defined as "intramolecularly cross-linked molecules that form a stable solution in many solvents", and their solutions exhibit low viscosity even at high concentrations and low temperatures. For example, the intrinsic viscosity of various microgels (M_w between 0.5×10^6 and 40×10^6), including styrene/DVB microgels, ranges between 4 and 8 mL/g, versus 160−3900 mL/g for linear polystryene.[4] This unique viscosity advantage of microgel polymers presents an opportunity to develop novel polymers for LPOS. We note that while the synthesis and properties of microgels have been investigated by several groups,[5] only one organic synthesis application of microgel polymers has been disclosed.[6] We have recently reported the preparation of novel microgel polymers and demonstrated their utility in the synthesis of a small array of oxazoles.[7] In this work, we investigated many of the important parameters to be considered when preparing microgels; such parameters are monomer concentration, cross-linker type, cross-linker content, reaction solvent, and reaction times. This led to the development of a chemically functionalized microgel with solubility and precipitation characteristics suitable for LPOS. The solubility properties of microgels allow reactions to occur in solution. Therefore, reactions using microgels can easily be monitored by standard solution-phase techniques such as NMR.

To demonstrate the versatility of these interesting polymers, we investigated the use of new microgels as a support for the preparation of a small library of phthalides and as a polymer-bound borohydride reducing reagent.

Results and Discussion

Microgel-Supported Phthalide Synthesis. The synthesis of phthalides contains a key reaction for testing a polymeric support: the ortho metalation of benzamide with butyllithium. The use of lithium anion chemistry on polymer support can be problematic; therefore, this chemistry is a good testing ground for the efficiency of new polymeric

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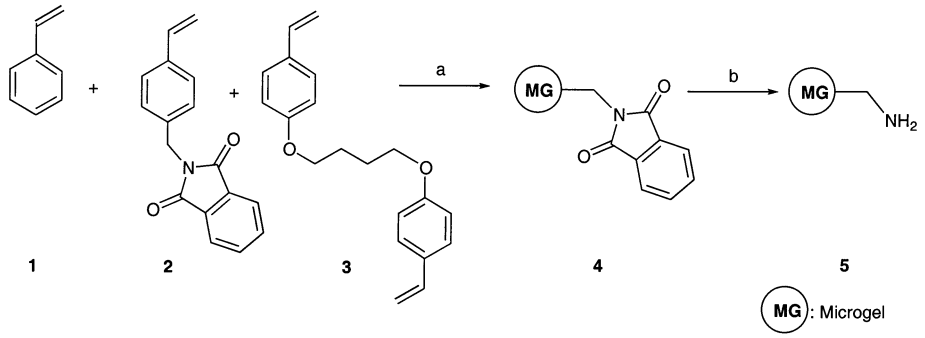
Scheme 1. Synthesis of Aminomethyl Microgel **5**[a]



[a] (a) 3 mol % AIBN, THF, 60 °C, 4 days; (b) hydrazine hydrate, dioxane 85 °C, 2 h.

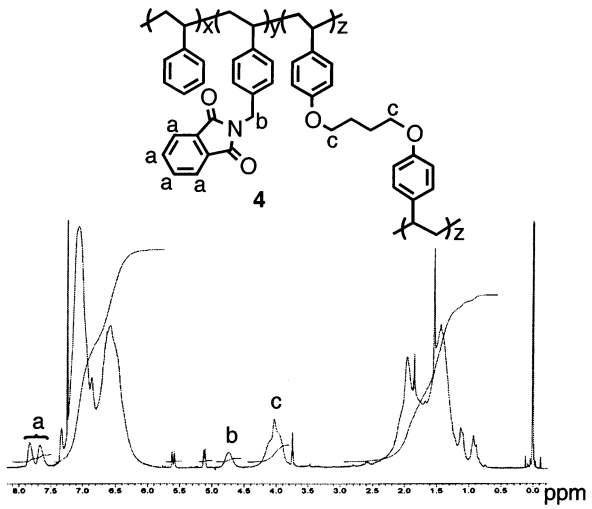


Figure 1. ^{1}H NMR spectrum of **4**.

supports. We have previously reported the preparation of a 24-member phthalide library using an insoluble polymer support.[8] *J*anda*J*els[8,9] provided improved results compared to some of the most broadly used polystyrene−divinylbenzene (PS−DVB) resins. Keeping these previous findings in mind, we used a similar synthetic scheme to prepare a phthalide library using a microgel polymer. An aminomethyl-supported microgel was prepared and utilized in the synthesis of the phthalides, and the results of the two resins (microgel-based versus *J*anda*J*el) were compared.

The two-step process for the preparation of aminomethyl microgel **5** is shown in Scheme 1. Microgel **4** was prepared by the AIBN-initiated radical polymerization of styrene **1**, *N*-(4-vinylbenzyl)phthalimide **2**, and 1,4-bis[4-(vinyl)phenoxy]butane **3** to provide polymer **4** in 55% yield. The number average molecular weight (M_n) and molecular weight distribution (M_w/M_n) of **4** were found to be 15 400 and 2.5, respectively (gel permation chromatography (GPC), calibrated by polystyrene standards). The ^{1}H NMR spectrum of **4** (Figure 1) shows the aromatic protons of phthalimide at 7.83 and 7.66 ppm (Figure 1, peak a) and methylene protons (−N−C*H*$_2$−) at 4.73 ppm (Figure 1, peak b). Methylene protons of cross-linker (−O−C*H*$_2$−CH$_2$−) were observed at 4.03 ppm (Figure 1c), while unreacted vinyl protons were observed at 5.60 and 5.11 ppm. On the basis of the ^{1}H NMR spectroscopic analysis, the calculated ratios (**1**/**2**/**3** = 89.8: 5:13.8) of the incorporated monomers in **4** were in agreement with that of the monomer feed (**1**/**2**/**3** = 100: 5:10). Thus,

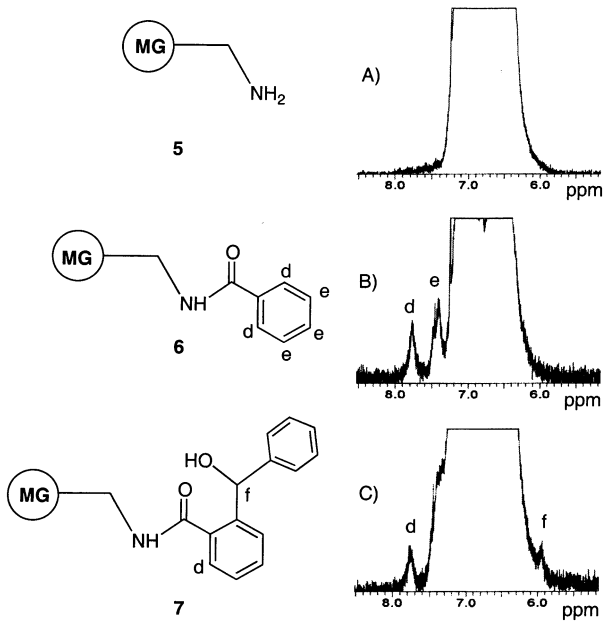
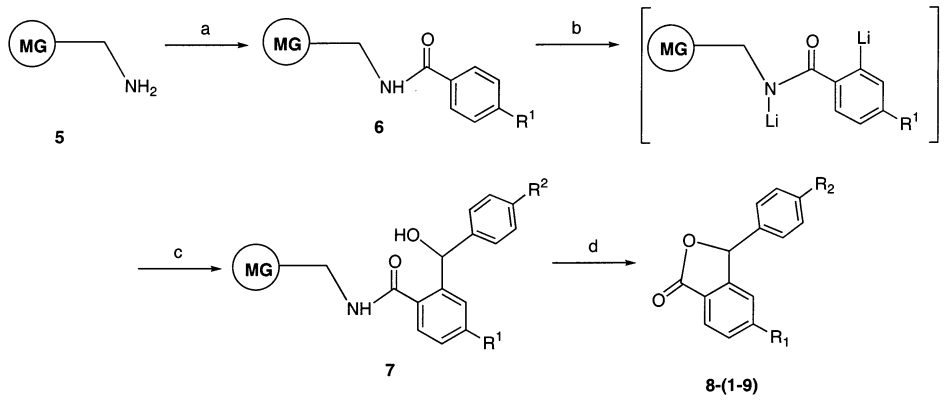


Figure 2. ^{1}H NMR spectrum of **5**−**7**.

the ^{1}H NMR spectrum of **4** was used to calculate the loading of phthalimide (0.34 mmol/g). To prepare **5** for library synthesis, the phthalimide was deprotected with hydrazine hydrate to give aminomethyl-functionalized microgel **5** in 92% isolated yield. The progress of this deprotection was monitored by using both IR and ^{1}H NMR spectroscopic analyses. No carbonyl group (1716 cm^{-1}) was observed in the IR spectrum. In the ^{1}H NMR spectrum, the aromatic protons of phthalimide at 7.83 and 7.66 ppm were not detected (Figure 2A). Microgels **4** and **5** were soluble in tetrahydrofuran (THF), toluene, methylene chloride, and *N*,*N*-dimethylformamide (DMF). We also found that microgel **5** was soluble in THF at −78 °C. These polymers were found to be insoluble in methanol and hexanes; thus, the microgel could be readily isolated by precipitation from methanol.

Microgel **5** was used for the synthesis of the phthalide library (Scheme 2). Aminomethyl microgel **5** was first acylated with benzoyl chloride in the presence of triethylamine to afford a polymer-bound benzamide **6** (R_1 = H) in 99% isolated yield. The ^{1}H NMR spectrum (Figure 2B) shows the appearance of the aromatic protons of benzamide at 7.77 and 7.41 ppm (peaks d and e). In the IR spectrum, a new peak due to a carbonyl group (1667 cm^{-1}) was also observed. Treatment of **6** with excess *n*-butyllithium followed by addition of excess benzaldehyde gave the microgel-bound

Scheme 2. Microgel-Supported Phthalide Synthesis[a]



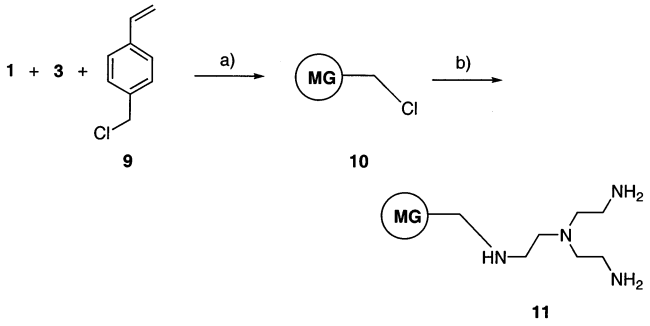
[a] (a) ArCOCl, Et_3N, THF, room temp, 30 min; (b) *n*-BuLi, THF, 0 °C, 5 min; (c) ArCHO, 0 °C, 30 min, then room temp, 1 h; (d) toluene, reflux, 16 h.

Table 1. Yield of Phthalides[a]

	$R^2 = H$	$R^2 = OMe$	$R^2 = Cl$
$R^1 = H$	90 (>99)	66 (>99)	77 (96)
$R^1 = OMe$	85 (93)	82 (>99)	71 (96)
$R^1 = Cl$	quant (97)	97 (98)	95 (95)

[a] Purities given in parentheses are estimated from GC analysis.

Scheme 3. Synthesis of Microgel-Supported Tris(2-aminoethyl)amine **11**[a]



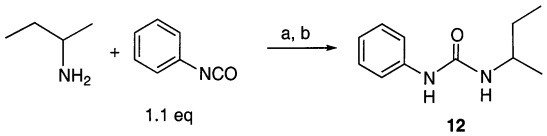
[a] (a) 3 mol % AIBN, THF, 60 °C, 4 days; (b) tris(2-aminoethyl)amine, THF, reflux, 20 h.

alcohol **7** (R_2 = H) in 99% isolated yield after precipitation from methanol. The ^{1}H NMR spectrum (Figure 2C) shows a small signal due to the methyne proton adjacent to the hydroxyl group at 5.94 ppm (peak f). Product **8-1** was cleaved from **7** by heating in toluene to obtain the desired phthalide compound in 90% yield and >99% purity as determined by GC analysis.

This methodology was also used to prepare eight additional phthalides (Table 1). The purity of the products was >93% in all cases, while the yields ranged from 66% to quantitative. On the basis of these results, it was concluded that the microgels were comparable in chemical reactivity to *J*anda*J*el resins.[8]

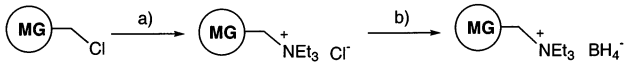
Microgel-Supported Scavenging Reagent. A tris(2-aminomethyl)amine-functionalized microgel **11** for scavenging applications was prepared according to the literature precedent for the preparation of insoluble scavenger resins.[10] First, chloromethyl-functionalized microgel **10** was prepared in 54% yield by the radical polymerization of styrene **1**, cross-linker **3**, and 4-vinylbenzyl chloride **9** as the functional monomer (Scheme 3). On the basis of ^{1}H NMR analysis, the ratio of the monomers incorporated in **10** were calculated to be (**1**/**9**/**3** = 58.3:5:8.5), resulting in a Cl loading of 0.54 mmol/g. The number average molecular weight (M_n) and molecular weight distribution (M_w/M_n) were found to be 15 400 and 2.5, respectively (GPC, calibrated by polystyrene standards). Chloromethyl-microgel **10** was treated with tris(2-aminoethyl)amine to obtain amine-supported microgel **11** in 86% isolated yield. The loading of tris(2-aminoethyl)amine was 0.42 mmol/g as determined by ^{1}H NMR spectroscopic analysis. Once again, polymers **10** and **11** were soluble in THF, toluene, methylene chloride, and DMF and could be reliably precipitated from methanol. We also found that microgel **10** was soluble in THF at −78 °C.

Scheme 4. Synthesis of a Urea Followed by Scavenging with Microgel Reagent **11**[a]



[a] (a) CH_2Cl_2, room temp, 1 h; (b) **11**, room temp, 1 h.

Scheme 5. Synthesis of Microgel-Supported Borohydride Reagent **14**[a]

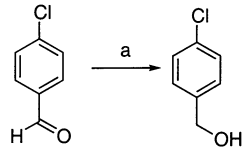


[a] (a) Et_3N, DMF, 65 °C, 16 h; (b) $NaBH_4$, THF, 60 °C, 14h.

The effectiveness of the tris(2-aminoethyl)amine microgel **11** for scavenging isocyanate was demonstrated as outlined in Scheme 4. An excess of phenyl isocyanate was added to *sec*-butylamine in methylene chloride. After 1 h, microgel **11** was added to the homogeneous solution to scavenge excess isocyanate. The microgel was precipitated with methanol and removed by filtration. When this procedure was used, no isocyanate contamination was detected in urea **12**, which was recovered in quantitative yield and 97% purity after concentration of the filtrate. It should be noted that for a similar reaction, using an insoluble scavenging reagent reported in the literature,[11] more equivalents of the scavenging reagent were needed as were extended reaction times.

Microgel as a Borohydride Reagent. Microgel-supported borohydride reagent **14** was prepared as outlined in Scheme 5. Chloromethyl-functionalized microgel **10** was reacted with excess triethylamine to prepare the quaternary salt, microgel **13**. Microgel **13** was recovered by precipitation from diethyl

Scheme 6. Reduction of an Aldehyde Using Microgel-Supported Reagent **14**[a]



15 **16**

[a] (a) **14** (1.1 equiv), THF, EtOH, room temp, 1 h.

ether in 86% yield. Since microgel **13** is partially soluble in methanol, and with hexane it forms a biphasic system with DMF, diethyl ether was chosen to precipitate the microgel **13** from the DMF solution. Previous research describes the preparation of an insoluble polymer-supported borohydride reagent (BER)[12] by treating ammonium chloride Amberlite ion-exchange resin with sodium borohydride in an aqueous solution.[13] However, because the microgel polymer shrinks and is insoluble in aqueous solution, it was not possible to exchange the chloride ion with borohydride in water. Thus, an alternative procedure where the chloride ion was exchanged with borohydride in THF at 60 °C using solid sodium borohydride was used to provide **14**.[14] Borohydride reagent **14** was recovered by precipitation from dilute aqueous NaOH, filtered, and isolated in 95% yield. Borohydrides are known to be stable in aqueous base,[15] and therefore, dilute NaOH solution was appropriate for the isolation of borohydride reagent **14**. Microgel **14** was soluble in THF, toluene, methylene chloride, and DMF but insoluble in hexane.

The effectiveness of microgel-bound borohydride reagent **14** was tested in the reduction of 4-chlorobenzaldehyde **15** (as a limiting reagent) to 4-chlorobenzyl alcohol **16** in THF/ethanol (Scheme 6). The loading of the borohydride resin was calculated to be 0.44 mmol/g based on the conversion of **15** to **16**. This was performed using **14** as the limiting reagent. When a slight excess of the microgel borohydride reagent, **14**, was used, complete conversion of **15** to **16** was observed. The spent reagent could then be removed by precipitation from hexane and the product recovered by evaporation of the solvent. The recovered product contained no starting material or polymeric byproducts as determined by GC and ^{1}H NMR analysis. Hexane was used instead of methanol to precipitate the polymer because this microgel was partly soluble in methanol.

Conclusion

In summary, three new applications of microgel polymers have been presented: (1) the construction of a phthalide library, (2) the preparation and use as a scavenger reagent, and (3) the preparation and application of a borohydride reagent. These three examples further demonstrate the potential of microgels in organic synthesis. It is noteworthy that in all cases the performance of the soluble polymeric microgels was shown to be equivalent to or better than insoluble cross-linked polymers. The preparation of the microgels is trivial and inexpensive. These polymers required no special equipment for reaction monitoring, which makes them attractive from a cost standpoint. Future studies will address the preparation of new microgel reagents and their use in organic synthesis.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-600, DRX-500, and a AMX-400 spectrometer using tetramethylsilane (TMS) as an internal standard. FT-IR spectra were obtained with a Nicolet Avatar 360 FT-IR spectrometer equipped with a Nicolet Smart Gate (ZnSe). Gel permeation chromatographic analyses (GPC) were carried out on a Shimadzu LC-6A preparative liquid chromatograph with a Shimadzu CR-501A integrator and a Shimadzu SPD-10AV UV−vis detector (254 nm) (Styragel HR2, HR3, and HR4, THF as eluent) using polystyrene standards. High-resolution mass spectra were obtained on an IonSpec MALDI−FTMS spectrometer. Gas chromatography (GC) analyses were carried out on HP-850 instrument using HP-1 (5 m × 0.53 mm × 2.65 μm column).

Preparation of Phthalimido-Protected Microgel 4. A mixture of **1** (13.7 g, 132 mmol), **2** (1.79 g, 6.8 mmol), **3** (4.00 g, 13.7 mmol), and AIBN (771 mg, 4.7 mmol, 3 mol %) was stirred in THF (390 mL) at 60 °C for 4 days under nitrogen. After cooling to room temperature, the reaction mixture was concentrated in vacuo to about 50 mL. The reaction mixture was poured into methanol (8 L). A white powdery polymer precipitated and was isolated by filtration. This polymer was redissolved in THF, reprecipitated in methanol, filtered, and dried in vacuo. The content of phthalimide unit was 0.34 mmol/g estimated by ^{1}H NMR. Yield: 10.7 g (55%).

4: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−), 3.9−4.2 (br, m, −O−C*H*$_2$−), 4.6−4.8 (br, s, −N−C*H*$_2$−), 5.11 (−CH=C*H*$_2$ trans, d, J = 10.6 Hz), 5.60 (−CH=C*H*$_2$ cis, d, J = 17.4 Hz), 6.0−7.3 (br, m, aromatics of styryl, −C*H*=CH$_2$), 7.66 (br, s, −N−CO−*Ar*, 2,5-H), 7.83 (br, s, −N−CO−*Ar*, 3,4-H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.1, 39−46, 67.3, 111.5, 114.0, 114.4, 125.6, 127.9, 130.3, 132.1, 133.9, 136.2, 145.3, 156.8, 158.8, 168.0 ppm; IR 3025, 2921, 2850, 1716, 1603, 1509, 1493, 1452, 1391, 1240, 1175, 1028, 828, 757, 698 cm^{-1}.

Preparation of Aminomethyl Microgel 5. Microgel **4** (1.0 g) was treated with $NH_2NH_2H_2O$ (205 mg, 6.4 mmol) in dioxane (10 mL) at 85 °C for 2 h. The reaction mixture was filtered, and the filtrate was poured into methanol (1 L). A white powdery polymer precipitated and was isolated by filtration and dried in vacuo. Yield: 880 mg (92%).

5: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−), 2.59 (br, d, J = 7.0 Hz), 3.7−4.2 (br, m, −NH$_2$−C*H*$_2$−, −O−C*H*$_2$−), 6.0−7.3 (br, m, aromatics) ppm; IR 3026, 2919, 1603, 1509, 1493, 1452, 1238, 1175, 1028, 828, 756, 697 cm^{-1}.

General Procedure for Phthalide Synthesis. Aminomethyl microgel **5** (100 mg, 0.035 mmol) was dissolved in THF (1.5 mL) and treated with triethylamine (1.5 equiv) and benzoyl chloride (1.5 equiv). After 1 h at room temperature, the reaction mixture was poured into methanol (100 mL). A white powdery polymer precipitated and was isolated by filtration and dried in vacuo. The obtained microgel **6** was

negative to a Kaiser amine test. Yield: 102 mg (99%). Microgel **6** (100 mg) was dissolved in THF (3 mL) at 0 °C under nitrogen, and *n*-BuLi (7 equiv, 2.5 M in pentane) was added to the solution. After 5 min, benzaldehyde (10 equiv) was added, and the reaction mixture was stirred at 0 °C for an additional 30 min. The reaction mixture was warmed to room temperature, and after 1 h, the solution was poured into methanol (100 mL). A white powdery polymer precipitated and was isolated by filtration and dried in vacuo. Yield: 102 mg (99%). The resulting microgel **7** was heated for 16 h at reflux in toluene, and the solution was poured into methanol (100 mL). A white powdery polymer precipitated and was isolated by membrane filtration, and the filtrate was concentrated in vacuo. The desired phthalide **8-1** was 99% pure as determined by GC analysis. Yield: 6.7 mg (90%).

6: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.7−2.4 (br, m −C*H*$_2$−C*H*-, −O−CH$_2$−C*H*$_2$−), 2.58 (br, d), 3.8−4.2 (br, m, −O−C*H*$_2$−), 4.55 (br, s, −NH−C*H*$_2$−), 6.0−7.3 (br, m, aromatics of styryl), 7.3−7.5 (br, m, −NH−CO−*Ar*, 3,4,5-H), 7.77 (br, s, −NH−CO−*Ar*, 2,6-H); IR 3025, 2921, 1667, 1603, 1509, 1493, 1452, 1239, 1176, 1028, 828, 757, 698 cm^{-1}.

7: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.7−2.4 (br, m −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−), 2.58 (br, d), 3.8−4.4 (br, m, −O−C*H*$_2$−), 4.4−4.7 (br, s, −NH−C*H*$_2$−), 5.8−7.5 (br, m, aromatics), 7.77 (br, s, −NH−CO−Ar, 2,6-H) ppm; IR: 3025, 2921, 1667, 1603, 1509, 1493, 1452, 1239, 1176, 1208, 827, 757, 698 cm^{-1}.

8-1: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.41 (s, 1H), 7.28 (m, 2H), 7.34 (dd, 1H, J = 7.7, 0.7 Hz), 7.37 (m, 3H), 7.56 (t, 1H, J = 7.3 Hz), 7.64 (dt, 1H, J = 7.3, 0.7 Hz), 7.97 (d, 1H, J = 7.3 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 82.7, 122.9, 125.6, 125.7, 127.0, 129.0, 129.3, 129.4, 134.3, 136.4, 149.7, 170.5 ppm; IR 2923, 1745, 1600, 1466, 1455, 1285, 1210, 965, 761, 739, 697, 688 cm^{-1}; HRMS calcd for $(M + H)^+$ 211.0754, found 211.0760.

Preparation of Chloromethyl Microgel 10. A mixture of **1** (14.1 g, 135 mmol), **9** (1.13 g, 7.4 mmol), **3** (4.00 g, 13.7 mmol), and AIBN (771 mg, 4.7 mmol, 3 mol %) was stirred in THF (390 mL) at 60 °C for 4 days under nitrogen. After reaching room temperature, the reaction mixture was evaporated to about 50 mL. The reaction mixture was poured into methanol (8 L). A white powdery polymer precipitated and was isolated by filtration. This polymer was redissolved in THF, reprecipitated in methanol, filtered, and dried in vacuo. The loading of the chloromethyl group was 0.54 mmol/g as estimated by ^{1}H NMR. Yield: 10.30 g (54%)

10: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−), 3.9−4.2 (br, m, −O−C*H*$_2$−), 4.4−4.6 (br, s, Cl−C*H*$_2$−), 5.12 (−CH=C*H*$_2$ trans, d, 1H, J = 11.0 Hz), 5.60 (−CH=C*H*$_2$ cis, d, 1H, J = 17.6 Hz), 6.0−7.3 (br, m, aromatics) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 26.0, 40−46, 67.5, 111.5, 113.9, 125.6, 127.9, 130.3, 136.2, 145.3, 156.9, 158.8 ppm; IR 3025, 2919, 2851, 1603, 1509, 1493, 1452, 1240, 1175, 1028, 828, 757, 698 cm^{-1}.

Preparation of Tris(2-aminoethyl)amine Microgel 11. A mixture of **10** (1.00 g, 0.54 mmol) and tris(2-aminoethyl)-amine (1.57 g, 10.7 mmol) was stirred in THF (10 mL) at room temperature for 20 h. The reaction mixture was poured into methanol (1 L). A white powdery polymer precipitated and was isolated by filtration and dried in vacuo. Yield: 0.90 g (86%). The loading of tris(2-aminoethyl)amine was 0.42 mmol/g as determined by ^{1}H NMR.

11: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−), 2.4−2.8 (br, m, −NH−C*H*$_2$−C*H*$_2$−N−), 3.6−3.8 (br, s, Cl−C*H*$_2$−), 3.8−4.2 (br, m, −O−C*H*$_2$−), 5.12 (−CH=C*H*$_2$ trans, d, 1H, J = 11.4 Hz), 5.60 (−CH=C*H*$_2$ cis, d, 1H, J = 18.0 Hz), 6.0−7.3 (br, m, aromatics, −C*H*=CH$_2$) ppm; IR 3026, 2919, 1603, 1509, 1493, 1452, 1239, 1175, 1028, 828, 757, 697 cm^{-1}.

Synthesis of 1-(*sec*-Butyl)-3-Phenylurea 12. To a solution of phenyl isocyanate (36 mg, 0.3 mmol) in dichloromethane (2 mL) was added *sec*-butylamine (20 mg, 0.27 mmol). The reaction mixture was agitated for 1 h, and **11** (50 mg, 0.021 mmol of tris(2-aminoethyl)amine) was added. After 1 h, the reaction mixture was poured into methanol (50 mL). A white powdery polymer precipitated and was isolated by membrane filtration, and the filtrate was concentrated in vacuo. Product **12** purity was 97% as determined by GC analysis. Yield: 54.0 mg (quantitative).

12: ^{1}H NMR($CDCl_3$, 500 MHz) δ 0.89 (t, 3H, −CH$_2$−C*H*$_3$, J = 7.5 Hz), 1.10 (d, 3H, −CH−C*H*$_3$, J = 6.6 Hz), 1.42 (m, 2H, −CH−C*H*$_2$), 3.78 (m, 1H, −NH−C*H*−), 5.18 (d, 1H, −CH−N*H*, J = 8.4 Hz), 7.01 (m, 1H, Ar 4-H), 7.18 (s, 1H, Ar−N*H*−), 7.26 (m, 4H, Ar 2-, 3-, 5-, 6-H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 10.4, 20.9, 30.0, 47.3, 120.4, 123.2, 129.1, 139.0 ppm; IR 3349, 3309, 2967, 2929, 1639, 1596, 1549, 1499, 1441, 1310, 1229, 1160 cm^{-1}; HRMS calcd for $C_{11}H_{17}N_2O$ 193.1335, found 193.1334.

Preparation of Microgel-Supported Ammonium Borohydride (14). The chloromethyl microgel **10** (2.00 g) was treated with triethylamine (1.19 mL) in DMF (10 mL) at 65 °C for 16 h. The reaction mixture was poured into diethyl ether (2 L). A brown powdery polymer precipitated and was isolated by filtration and dried in vacuo. Yield of **13**: 1.81 g (86%). The triethylammonium chloride microgel **13** (1.10 g) was treated with sodium borohydride (223 mg) in THF (30 mL) at 60 °C for 14 h. The reaction mixture was poured into 0.2% NaOH(aq) (2 L). A white powdery polymer precipitated and was filtered and dried in vacuo. Yield of **14**: 1.03 g (95%).

13: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−, −N− CH$_2$−C*H*$_3$), 3.1−3.4 (s, −N−C*H*$_2$−CH$_3$), 3.8−4.2 (br, m, −O−C*H*$_2$−), 4.3−4.8 (br, s, Ar−C*H*$_2$−N), 5.12 (−CH=C*H*$_2$ trans, d, J = 11.4 Hz), 5.60 (−CH=C*H*$_2$ cis, d, J = 18.0 Hz), 6.0−7.3 (br, m, aromatics, −C*H*=CH$_2$) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 8.3, 26.0, 39−46, 52.6, 65.8, 111.5, 113.9, 114.4, 125.5, 127.3, 127.9, 130.3, 136.1, 144.7, 156.9, 158.7 ppm; IR 3358, 3024, 2917, 2647, 2324, 1603, 1492, 1451, 1238, 1174, 1027, 827, 756, 697 cm^{-1}.

14: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.8−2.4 (br, m, −C*H*$_2$−C*H*−, −O−CH$_2$−C*H*$_2$−, −N−CH$_2$−C*H*$_3$), 3.1−3.4 (s, −N−C*H*$_2$−CH$_3$), 3.8−4.2 (br, m, −O−C*H*$_2$−), 4.3−4.8 (br, s, Ar−C*H*$_2$−N), 5.12 (−CH=C*H*$_2$ trans, d, J = 11.4 Hz), 5.60 (−CH=C*H*$_2$ cis, d, J = 18.0 Hz), 6.0−7.3 (br, m, aromatics, −C*H*=CH$_2$) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz)

δ ppm; IR 3426, 3025, 2918, 2324, 2287, 1603, 1509, 1492, 1450, 1240, 1175, 1070, 1028, 828, 757, 698 cm^{-1}.

Reduction of 4-Chlorobenzaldehyde (15). 4-Chlorobenzaldehyde **15** (56 mg, 0.40 mmol) was added to a THF/EtOH (10/2.5 mL) solution of **14** (500 mg) and stirred at room temperature for 1 h. The solution was added to hexane (500 mL), and the precipitated polymer was removed by Celite filtration. The filtrate was evaporated and dried in vacuo. Yield: 40 mg (71%). Purity: >99% (GC).

16: ^{1}H NMR($CDCl_3$, 600 MHz) δ 4.67 (s, 2H, $-CH_2-$OH), 7.32 (m, 4H, aromatics); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 64.6, 128.3, 128.7, 133.4, 139.2 ppm.

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