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Synthesis and Characterization of Novel pH-Responsive Microgels Based on Tertiary Amine Methacrylates

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Emulsion polymerization of 2-(diethylamino)ethyl methacrylate (DEA) in the presence of a bifunctional cross-linker at pH 8−9 afforded novel pH-responsive microgels of 250−700 nm diameter. Both batch and semicontinuous syntheses were explored using thermal and redox initiators. Various strategies were evaluated for achieving colloidal stability, including charge stabilization, surfactant stabilization, and steric stabilization. The latter proved to be the most convenient and effective, and three types of well-defined reactive macromonomers were examined, namely, monomethoxy-capped poly(ethylene glycol) methacrylate (PEGMA), styrene-capped poly[2-(dimethylamino)ethyl methacrylate] ($PDMA_{50}$-St), and partially quaternized styrene-capped poly[2-(dimethylamino)ethyl methacrylate] ($10qPDMA_{50}$-St). The resulting microgels were pH-responsive, as expected. Dynamic light scattering and ^{1}H NMR studies confirmed that reversible swelling occurred at low pH due to protonation of the tertiary amine groups on the DEA residues. The critical pH for this latex-to-microgel transition was around pH 6.5−7.0, which corresponds approximately to the known pK_a of 7.0−7.3 for linear PDEA homopolymer. The microgel particles were further characterized by electron microscopy and aqueous electrophoresis studies. Their swelling and deswelling kinetics were investigated by turbidimetry. The PDEA-based microgels were compared to poly-[2-(diisopropylamino)ethyl methacrylate] (PDPA) microgels prepared with identical macromonomer stabilizers. These PDPA-based microgels had a lower critical swelling pH of around pH 5.0−5.5, which correlates with the lower pK_a of PDPA homopolymer. In addition, the kinetics of swelling for the PDPA microgels was somewhat slower than that observed for PDEA microgels; presumably this is related to the greater hydrophobic character of the former particles.

Introduction

Increasing attention is being paid to the synthesis and applications of novel stimulus-responsive microgels. Poly(*N*-isopropylacrylamide) (PNIPAM) is perhaps the most studied example; these microgels are normally prepared by aqueous dispersion polymerization at around 70 °C and exhibit thermoresponsive behavior.[1−5] Above 32 °C, the lightly cross-linked PNIPAM particles exist in their nonsolvated latex-like form, but at room temperature the particles become hydrophilic and acquire microgel character, often swelling by more than an order of magnitude in size. This thermal transition can be raised or lowered by copolymerizing a suitable hydrophilic or hydrophobic comonomer with the NIPAM.[6] The temperature-dependent binding of proteins onto PNIPAM-based microgels has been noted by Kawaguchi and co-workers[7] and their use as recyclable sequestrators for heavy metals has been suggested.[8] Detailed temperature-dependent rheological studies have also been reported by Kiminta and Luckham.[9]

There are also many examples of pH-responsive microgels. For example, alkali-swellable latexes based on (meth)acrylic acid find widespread use in various industrial applications, such as thickeners for cosmetic and pharmaceutical formulations.[10] Saunders et al. reported the pH-induced swelling behavior of poly(methyl methacrylate-*stat*-methacrylic acid) latexes and the deswelling effects of adding lower alcohols and poly(ethylene oxide).[11] However, there have been relatively few academic studies of *acid*-swellable microgels. In 1992 Ma and Fukutomi[12] reported the synthesis of near-monodisperse poly(4-vinylpyridine)-based (P4VP) latex and the production of robust, ordered microgel films by chemical cross-linking via quaternization. One application suggested for such microgel-based coatings was a new stationary phase for

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liquid chromatography.[13] Similarly, Loxley and Vincent[14] examined the synthesis and acid-swelling behavior of poly(2-vinylpyridine)-based (P2VP) microgels. The extent of swelling of these microgels in a pH 3.8 buffer was monitored in real time using a stopped-flow technique. It was found that higher levels of styrene comonomer reduced the extent of swelling and increased the time required for maximum swelling. However, the degree of cross-linking had surprisingly little effect on the rate of swelling. Very recently Kuckling et al. reported the synthesis of so-called "nanogels" that comprise both thermoresponsive poly-NIPAM cores and pH-responsive P2VP-based coronas.[15] These fascinating nanoparticles were prepared by UV-induced cross-linking of terpolymers containing pendent dimethylmaleinimide groups. Finally, Murthy and co-workers have described the synthesis of acrylamide-based microgels via inverse emulsion polymerization and evaluated their performance as delivery vehicles for protein-loaded vaccines.[16]

Herein we describe the synthesis and characterization of a new class of acid-swellable, sterically stabilized microgel particles based on 2-(diethylamino)ethyl methacrylate (DEA) or 2-(diisopropylamino)ethyl methacrylate (DPA). Since the pK_a of DEA homopolymer (PDEA) is around pH 7.0−7.3, the DEA-based microgels should swell at around physiological pH, which suggests potential biomedical applications. In contrast, the pK_a of PDPA is close to pH 6[17] and the pK_a values for P4VP and P2VP are around 3 and 5, respectively.[18] Therefore microgels based on P2VP and P4VP only swell in relatively acidic solutions.[14] Moreover, P4VP and P2VP have high glass transition temperatures (T_g > 100 °C),[19] which means that poly(vinylpyridine)-based microgels are relatively rigid particles and have poor film-forming properties. In contrast, the T_g of PDEA is only around 16 °C,[20] and chemical intuition suggests that the T_g of PDPA should be lower than this value. Thus these new tertiary amine methacrylate-based microgels should be relatively soft and are expected to spread easily during adsorption at the solid−water interface. In view of these distinctive physical characteristics, we felt that a detailed investigation of such film-forming microgels was warranted.

Experimental Section

Materials. 2-(Diethylamino)ethyl methacrylate (DEA) (Aldrich), poly(propylene glycol) diacrylate (PPGDA) (Aldrich), and 2-(diisopropylamino)ethyl methacrylate (DPA) (Scientific Polymer Products, USA) were treated with basic alumina in order to remove inhibitor. Sodium bicarbonate, sodium dodecyl sulfate (SDS), ammonium persulfate (APS), *N*, *N*, *N*′, *N*′-tetramethylethylenediamine (TEMED), and 4,4′-azobis(4-cyanovaleric acid) (ACVA) were used as received. Monomethoxy-capped poly(ethylene glycol) methacrylate (PEGMA) macromonomer (M_n = 2000; M_w/M_n = 1.10) was supplied by Cognis Performance Chemicals (Hythe, U.K.) as a 50 wt % aqueous solution. Doubly distilled deionized water was used in all the polymerizations.

Macromonomer Syntheses Using Oxyanionic Polymerization. The DMA-based macromonomer ($PDMA_{50}$-St) was prepared using oxyanionic polymerization as described previously.[12] The degree of polymerization was estimated to be 50 by NMR (corresponding to an M_n of approximately 8000). Gel permeation chromatography analysis using poly(methyl methacrylate) calibration standards indicated an M_n of 6700 and an M_w/M_n of 1.23. For some microgel syntheses, this macromonomer was partially quaternized using methyl iodide in THF at 20 °C as described previously.[21] According to ^{1}H NMR studies this protocol led to approximately 10 mol % of the DMA residues being quaternized, which was close to the target degree of quaternization; this derivatized macromonomer is denoted "10q$PDMA_{50}$-St".

Microgel Syntheses via Emulsion Polymerization. Polymerizations were carried out in a 250 mL round-bottomed flask, fitted with a nitrogen gas inlet, water condenser, and an overhead mechanical stirrer operating at 250 rpm using a "flat anchor" type stirrer. Most reactions were carried out at 10 wt % solids, but selected syntheses were performed at 20 wt %. For 10 wt % batch reactions using APS initiator, the required amount of water (typically 85 g) and a mixture (typically 10.5 g) of DEA (or DPA) and PPGDA cross-linker were added to the flask and the solution was stirred for 30 min under nitrogen flow at 70 °C. The polymerization commenced on addition of a previously degassed aqueous solution (typically 5.0 g) of the initiator (1.0 wt % based on monomer). Several initiators were examined, including APS at 70 °C, ACVA at 70 °C, and 1:1 APS/TEMED at 25 °C. In the case of the ACVA initiator, sodium bicarbonate was used to adjust the solution pH. Syntheses at 20 wt % solids were conducted in batch mode using APS initiator and PPGDA cross-linker (both were used at 1.0 wt % based on monomer). When a reactive macromonomer stabilizer was used, the required amount (10.0 wt % based on monomer) was added to the aqueous solution prior to the addition of the monomer and cross-linker. In addition, PDEA latex without any cross-linker was prepared as described above for use as a reference in the pH-induced swelling/deswelling experiments.

Surfactant and Charge-Stabilized Microgels. SDS (either 1.5 or 3.0 wt % based on monomer as the sole surfactant or 1.0 wt % based on monomer as cosurfactant) was added to some syntheses to enhance colloidal stability. Excess surfactant was eliminated by ultrafiltration of the latexes at pH 9 (i.e., in their nonmicrogel form). In addition, a charge-stabilized PDEA microgel was synthesized in the absence of any surfactant; this dispersion was stabilized by anionic sulfate groups derived from the APS initiator.

Sterically Stabilized Microgels Using Macromonomers. PEGMA macromonomer was evaluated as a reactive steric stabilizer in both PDEA and PDPA microgel syntheses. The styrene-capped DMA macromonomer ($PDMA_{50}$-St) was also used as a reactive steric stabilizer in the syntheses of DEA-based microgel latexes. However, in this case the reactions were performed at 25 °C using the 1:1 APS/TEMED redox initiator, since the cloud point of the $PDMA_{50}$-St macromonomer was around 40 °C at pH 8. Monomer-starved reaction conditions were used to avoid coagulation during synthesis. A mixture of DEA, PPGDA, and TEMED was fed into an aqueous solution containing SDS and APS over a 4 h period at a stirring rate of 180 rpm. The analogous batch reaction with SDS produced macroscopic precipitation, as did monomer feeding in the absence of SDS. Both monomer feeding and the addition of SDS appear to be essential for producing stable microgels when using the $PDMA_{50}$-St macromonomer at ambient temperature.

Stable PDEA and PDPA microgels were obtained with only a small amount (<6%) of coagulum when using the 10q$PDMA_{50}$-St stabilizer at 10 wt % relative to monomer. In all syntheses the reaction solution turned milky-white within 5−10 min and was stirred for 16−20 h at 70 °C under a nitrogen atmosphere.

Purification of Microgels. Serum replacement (ultrafiltration) was used to eliminate excess stabilizer and/or SDS, as well as traces of monomer and initiator, to purify the PDEA and PDPA latex particles. Ultrafiltration was performed using a Molecular/Por stirred Spectrum cell (400 mL) by replacing the serum with water in continuous mode; this serum was periodically collected to assess the extent of purification. Purification was

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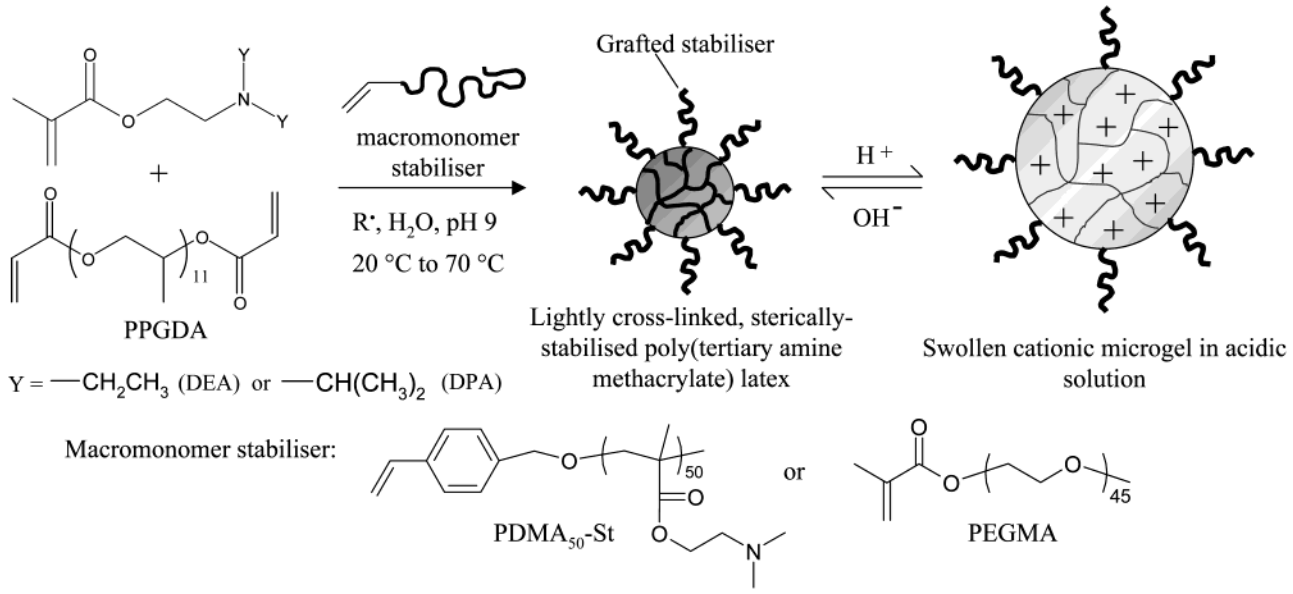

Figure 1. Schematic representation of the emulsion polymerization synthesis and subsequent acid-induced swelling of the poly(tertiary amine methacrylate)-based microgels described in this study.

continued until the serum surface tension (Du Nouy ring, Kruss K10 instrument) was close to that of pure water (68−72 mN·m^{-1}). In some cases dialysis tubing (Spectra Por Biotech, PVDF membrane with a molecular weight cutoff of 500 000) was used prior to ultrafiltration. This purification process can take up to 1 month, depending on the volume of microgel to be purified and the extent of pore blockage by the microgel. Nevertheless, ultrafiltration is preferred to centrifugation because the film-forming nature of these microgel latexes makes their redispersion very difficult.

Microgel Characterization. All solutions were prepared using doubly distilled deionized water that had been filtered (Whatman 200 nm nylon filter) prior to use. If required, pH adjustments were made using either HCl or NaOH. All measurements were made on dispersions that had equilibrated for 30−90 min at the appropriate pH. Significant pH drift was observed for most microgels on longer time scales (hours). NaCl was used as the background electrolyte in all experiments.

^{1}H NMR Spectroscopy. Selected dried PEGMA-stabilized microgels were dissolved in $CDCl_3$. Alternatively, the microgel was centrifuged, the decanted supernatant was replaced by D_2O, and the pH was adjusted using DCl or NaOD. ^{1}H NMR spectra were recorded using a 300 MHz Bruker Avance DPX 300 spectrometer. The integrated intensity of the relatively weak signal at δ 3.8−4.0 ppm due to the two oxymethylene protons adjacent to the ester groups of the DEA or DPA residues was compared to that of the oxyethylene proton signal due to the PEGMA stabilizer at δ 3.5−3.6 in order to estimate the PEGMA stabilizer content of the microgel particles.

The $PDMA_{50}$-St/PDEA microgel was dissolved in D_2O/DCl at low pH. For estimation of the $PDMA_{50}$-St stabilizer content, the signal at δ 2.5 due to the dimethylamino protons of the DMA residues was compared to the signal at δ 3.8−4.0 due to the two oxymethylene protons adjacent to the ester groups of the DEA residues. A similar approach was used to assess the incorporation of the 10q$PDMA_{50}$-St stabilizer within the microgels.

Scanning Electron Microscopy. Micrographs were obtained using a Leo Stereoscan 420 instrument operating at 10 kV and 15 pA equipped with an Emitech K1150 cryogenic system. The microgels were equilibrated in their latex form at pH 9 prior to being frozen in a liquid nitrogen slush, fractured, and then etched for 5 min at −100 °C. Samples were then sputter-coated with a thin overlayer of gold prior to inspection to prevent sample-charging effects.

Dynamic Light Scattering. Hydrodynamic particle diameters were measured at 20 °C using a Brookhaven BI-200SM instrument equipped with a solid-state laser operating at 532 nm and 125 mW. The scattered light was detected normal to the incident laser source, and the mean particle diameter was calculated using the Stokes−Einstein equation from the quadratic fitting of the correlation function, with typical analysis times of 20−30 min. These measurements were performed in triplicate on dilute aqueous dispersions (0.005−0.25 wt %) using 0.005 M NaCl as background electrolyte.

Aqueous Electrophoresis. Zeta potentials were calculated from the measured electrophoretic mobilities using a Malvern Instruments ZetamasterS instrument. Measurements (averaged over 20 runs) were made as a function of pH on dilute dispersions (0.012−0.05 wt %) in 0.005 M NaCl by gradually adding HCl to induce the latex-to-microgel transition in dispersions equilibrated overnight at about pH 10.

Kinetics of Microgel Swelling/Deswelling. The kinetics of microgel (de)swelling experiments were performed by turbidimetry: the change in transmittance at 500 nm was monitored over time for 0.05 wt % dispersions using a Perkin-Elmer Lambda 25 spectrometer. Dilute (0.05−0.1 M) HCl (or NaOH) was added to adjust the solution pH to 3.5−4.5 (or pH 8−9).

Results and Discussion

The synthesis parameters and physicochemical properties of the PDEA and PDPA microgels prepared using the poly(propylene glycol) diacrylate cross-linker (see Figure 1) are summarized in Table 1. The charge- and surfactant-stabilized microgels are listed first, followed by the sterically stabilized microgels. The abbreviations indicate both the nature of the microgel (either PDEA or PDPA) and the type of surfactant/polymeric stabilizer. Sterically stabilized acid-swellable microgels were of particular interest to us because there has been relatively little academic work in this area. This is somewhat surprising, since steric stabilization offers the best prospect of developing microgel syntheses at high solids. In this context, it is noteworthy that the pH-responsive microgels reported by Loxley and Vincent[14] were synthesized at only 1% solids, which is much too low to be feasible on an industrial scale.

There are many electron microscopy studies of stimulus-responsive high T_g microgels such as PNIPAM, P4VP, or P2VP in the literature.[1,11,12,14,22] In contrast, electron microscopy studies of the morphology of the tertiary amine methacrylate-based microgels proved somewhat problematic due to their soft, film-forming nature. Various

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Table 1. Summary of the Synthesis Conditions and Physicochemical Data for the Various Tertiary Amine Methacrylate-Based Microgels Synthesized in This Study

entry no.	microgel type[a] (stabilizer/core)	SDS(wt %)	initiator type	synthesis temp (°C)	stabilizer content (wt %)	latex diameter[b] (nm)	volumetric swelling factor[c]	critical swelling pH	IEP[d]
1	non-cross-linked PDEA	0	APS	70	N/A	150	N/A	N/A	8.0
2	charge-stabilized PDEA	0	APS	70	N/A	700	7	7.0−7.4	7.8
3	SDS/PDEA	1.5	ACVA	70	N/A	260	6	5.0−6.6	7.2
4	PEGMA/PDEA	0	APS	70	7.1	280	37	6.3−6.6	7.6
5	$PDMA_{50}$-St/PDEA	1	APS/TEMED	25	4.9	455	20	6.5−7.0	9.2
6	$10qPDMA_{50}$-St/PDEA	0	ACVA	70	6.1	250	9	6.0−7.6	7.4
7	PEGMA/PDPA	0	APS	70	6.8	315	49	5.2−5.4	6.8
8	$10qPDMA_{50}$-St/PDPA	0	ACVA	70	4.5	1300	>9	5.2−5.5	9.3

[a] PPGDA was used as cross-linker at 1.0 wt % in all cases except the non-cross-linked PDEA latex (entry 1). [b] Measured at pH 9, except for entries 2, 6, and 8 where a local minimum in diameter was observed. In these three cases the minimum diameter at alkaline pH is cited. [c] Based on the ratio of the swollen microgel diameter at pH 4 to the latex diameter at alkaline pH. [d] Determined by aqueous electrophoresis measurements.

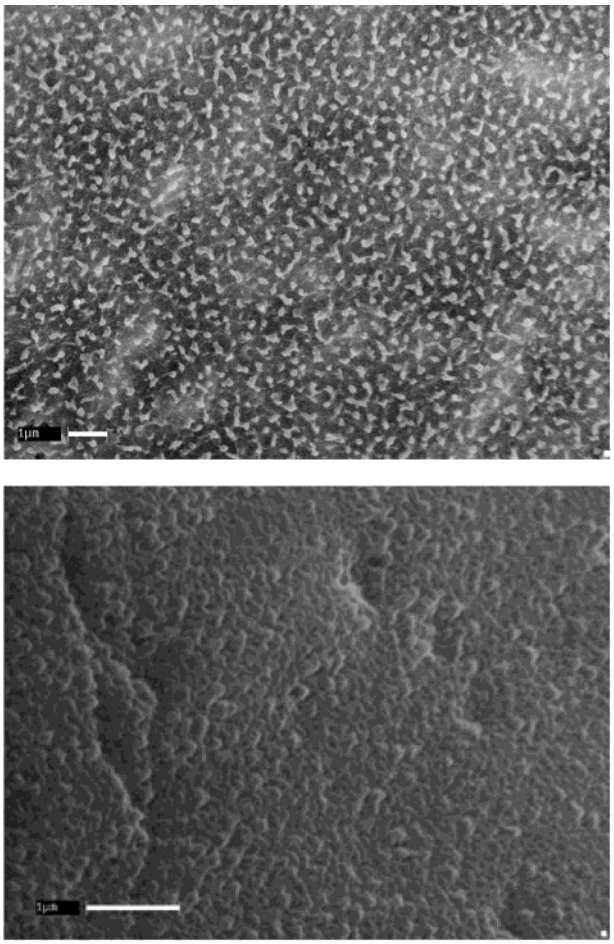

Figure 2. The upper image of a $10qPDMA_{50}$-St/PDPA microgel was obtained by conventional scanning electron microscopy. The microgel was spread onto a glass slide from a 0.05 wt % dispersion at pH 9. The lower image is a PEGMA-stabilized PDEA microgel using cryoSEM sample preparation techniques to prevent film formation (the scale bars are 1 μm in both cases).

sample preparation protocols were evaluated, using both conventional SEM and cryoSEM techniques. A scanning electron micrograph of the diluted $10qPDMA_{50}$-St/PDPA microgel obtained using conventional scanning electron microscopy (SEM) preparation techniques is shown in Figure 2a. This image was obtained by simply spreading the diluted aqueous microgel over the specimen stub in order to obtain isolated particles and hence minimize particle coalescence. However, this approach was not entirely successful: nonspherical submicrometer-sized

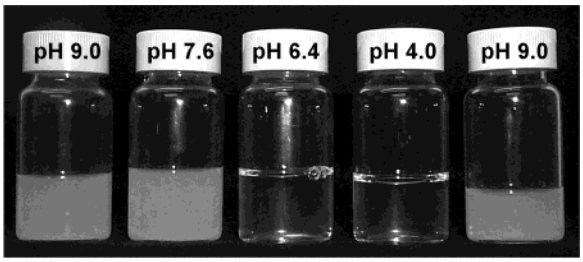

Figure 3. Digital photographs of $PDMA_{50}$-St/PDEA microgel dispersions at 0.05 wt % in 0.005 M NaCl. The solution pH was lowered from pH 9 (latex form) to pH 4 (transparent microgel form) and then returned to pH 9. Visual inspection indicated the apparent reversibility of the swelling transition, but turbidimetry studies revealed hysteresis effects.

features are also observed which correspond to partially coalesced particles. Nevertheless, the size distribution of these features is reasonably uniform. The PDEA microgels have a slightly higher T_g than the PDPA microgels and are correspondingly easier to study. A typical cryoSEM image for the PEGMA/PDEA microgel (entry 4 in Table 1) is shown in Figure 2b. While the expected spherical morphology is not readily discernible, there is some evidence for pseudospherical features with mean dimensions of approximately 150−250 nm. This is somewhat less than the dynamic light scattering (DLS) diameter of 280 nm reported in Table 1. However, DLS tends to oversize relative to electron microscopy for size distributions with finite polydispersities (the typical polydispersities of the various microgels listed in Table 1 ranged from 0.13 to 0.30, with most examples falling within the 0.17−0.24 range). Moreover, the former technique reports a hydrodynamic diameter that necessarily includes the thickness of the steric stabilizer layer, so oversizing relative to electron microscopy is to be expected.

All the microgels in Table 1 were synthesized as milky-white dispersions (i.e., in their nonsolvated latex form) at alkaline pH. This is illustrated in Figure 3 for the $PDMA_{50}$-St/PDEA microgel at pH 9. On addition of acid, the DEA residues become protonated and this dispersion quickly became optically transparent below pH 7.0 due to microgel swelling. On addition of alkali, visual inspection indicated that the transparent solutions quickly became turbid at pH 9, suggesting the *apparent* reversibility of the microgel-to-latex deswelling transition. However, more quantitative turbidimetry measurements indicated that significant hysteresis effects occurred during deswelling (see later). Most of the microgels could be subjected to at least three pH cycles (between pH 9 and pH 4) without causing salt-induced flocculation.

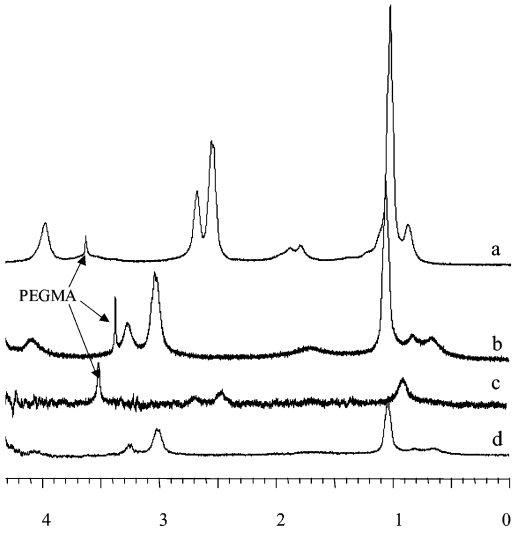

Figure 4. ^{1}H NMR spectra of selected DEA-based microgels: (a) PEGMA-stabilized PDEA-microgel in $CDCl_3$; (b) PEGMA-stabilized PDEA-microgel in D_2O at pH 2; (c) PEGMA-stabilized PDEA-microgel in D_2O at pH 10; (d) charge-stabilized PDEA microgel in D_2O at pH 2.

It is perhaps worth emphasizing that the *linear* (non-cross-linked) PDEA latex prepared at pH 9 simply *dissolved* in acidic solution: on returning to pH 9, the polymer chains precipitated from solution. This control experiment confirms that cross-linking is essential for the protonated PDEA chains to "remember" their former latex form. In our initial microgel syntheses we used ethylene glycol dimethacrylate (EGDMA) as a cross-linker, but this proved unsatisfactory since precipitation was observed during the microgel-to-latex deswelling transition. Much better reversibility during pH cycling was achieved using the poly(propylene glycol) diacrylate cross-linker, which was used to prepare all of the microgels listed in Table 1. The reason for this difference is unclear, but the lower water solubility of the diacrylate cross-linker may be relevant, since this should ensure better partitioning with the tertiary amine methacrylate monomer (DEA or DPA). Alternatively, EGDMA appears to be prone to intrachain cyclization, which may compromise its effectiveness as a cross-linker.[23]

Incorporation of Steric Stabilizers. The stabilizer contents of the PDEA- and PDPA-based microgels were determined by ^{1}H NMR spectroscopy and are listed in Table 1. For example, Figure 4a shows the ^{1}H NMR spectrum of the PEGMA-stabilized PDEA microgel in $CDCl_3$. The signal at δ 3.6 is due to the oxyethylene protons; comparison of this peak integral with that of the signal at δ 4.0 due to the two oxymethylene protons adjacent to the ester group of the DEA residues enabled the PEGMA stabilizer content of this microgel to be assessed. However, the microgels prepared using the $PDMA_{50}$-St and 10qP-DMA_{50}-St macromonomers were only poorly soluble in $CDCl_3$ and hence required a different approach. These microgels were dissolved in DCl/D_2O, which ensured protonation (and hence full solvation) of both the PDMA-based stabilizer and the lightly cross-linked PDEA (or PDPA) cores. The signals at δ 2.6 due to the dimethylamino protons of the PDMA stabilizer were compared to those due to the oxyethylene protons at δ 4.0 (shifted due to protonation of the amine residues) to estimate the stabilizer contents of these microgels. In our synthetic work we focused on producing as wide a range of different microgels as possible. Thus a number of synthesis parameters (stabilizer type, initiator type, synthesis temperature, etc.) were varied, and it is not possible to make meaningful correlations between stabilizer contents and latex diameters for the microgels presented in Table 1. Instead, each microgel example should be treated individually.

^{1}H NMR spectroscopy can also be used to monitor the chemical changes that occur during the microgel-to-latex transition. Figure 4b shows a ^{1}H NMR spectrum recorded in D_2O/DCl at pH 2 for a PEGMA-stabilized PDEA microgel (see entry 4 in Table 1). Under these conditions the particles are in their highly swollen form and each of the expected signals for the protonated DEA residues and the PEGMA stabilizer is visible (this stabilizer signal was assigned by reference to the ^{1}H NMR spectrum recorded for the charge-stabilized PDEA microgel at pH 2, see Figure 4d). However, when the pH was adjusted to 10 (see Figure 4c), the DEA residues become deprotonated and hence hydrophobic, leading to strong signal attenuation. In contrast, the signal at δ 3.5−3.6 due to the solvated PEGMA stabilizer is clearly visible in alkaline media.

The PEGMA stabilizer contents were similar for the PDEA and PDPA microgels. A PEGMA content of 7.1% provided adequate colloidal stabilization for the PDEA microgel (entry 4 in Table 1), since no flocculation occurred over the pH range studied. However, a PDPA microgel containing 6.8% PEGMA (entry 7 in Table 1) formed small flocs between pH 5.7 and pH 9. Given the similar latex sizes and stabilizer contents, this reduced stability must be due either to a lower surface concentration of the PEGMA stabilizer and/or to stronger van de Waals attractions between the more hydrophobic PDPA latex particles. It is also noteworthy that no flocculation was observed for the $PDMA_{50}$-St-stabilized PDEA microgel, which contained 4.9% $PDMA_{50}$-St stabilizer. In this case the polyelectrolytic nature of the stabilizer imparts additional electrosteric stabilization at low pH, which presumably accounts for its excellent colloid stability.

The stabilizer content of the 10qDMA_{50}-St/PDEA microgel is 6.1%, which is higher than that obtained for the nonquaternized macromonomer (4.9%). However, the presence of flocs close to the isoelectric point (IEP) indicates inefficient stabilization. This is probably due either to patchy coverage or to some fraction of the stabilizer chains being buried within the particles (and thus not being available for colloidal stabilization). According to our ^{1}H NMR data, the same 10qDMA_{50}-St stabilizer is incorporated less efficiently during the DPA polymerization. However, the greater difference in hydrophobicity between the PDPA and the stabilizer should lead to more efficient partitioning of the stabilizer at the latex surface. Thus colloidal stability was achieved with a lower stabilizer content (only 4.5%) than those obtained for either the PEGMA/PDPA or the 10qDMA_{50}-St/PDEA microgels.

Physical Characterization. Table 1 shows the critical swelling pH, the volumetric swelling factor (i.e., the cube of the ratio of the microgel diameter at pH 4 to that of the latex diameter at alkaline pH), and the mean latex diameters for all microgels. The change in mean hydrodynamic diameter that occurs due to the latex-to-microgel transition is shown in Figure 5 for three selected microgels (entries 4, 5, and 7 in Table 1). The critical swelling pH falls into two distinct ranges, depending on whether the microgel comprises PDEA or PDPA chains (compare, for example, the PEGMA/PDEA and PEGMA/PDPA data shown in Figure 5). This is in reasonably good agreement with the pK_a values of 6.0 and 7.3 reported for linear PDEA

(23) Landin, D. T.; Macosko, C. W. *Macromolecules* **1988**, *21*, 846.

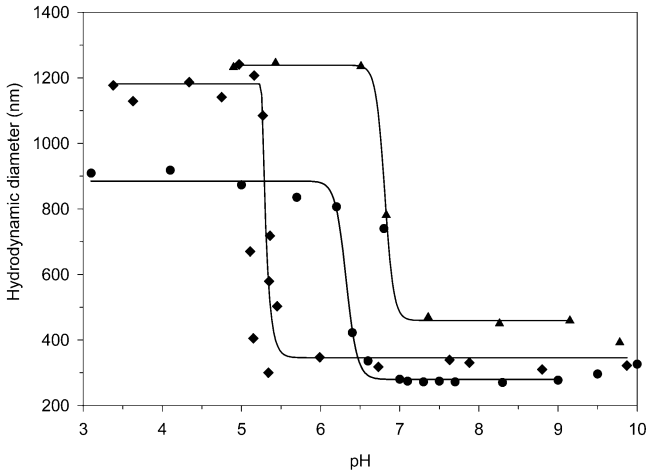

Figure 5. Variation of mean hydrodynamic diameter with pH for selected microgels: $PDMA_{50}$-St/PDEA (▲) 0.035 wt %; PEGMA/PDEA (●) 0.25 and 0.05 wt %; PEGMA/PDPA (◆) 0.16 and 0.005 wt %. The data are averaged over three runs and the solid lines are a guide to the eye, rather than a fit to the data.

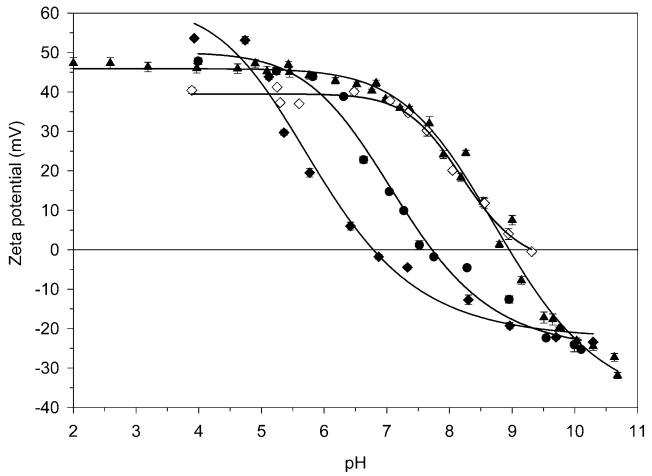

Figure 6. Zeta potential vs pH curves obtained for selected microgels: $PDMA_{50}$-St/PDEA (▲) 0.035 wt %; PEGMA/PDEA (●) 0.05 wt %; PEGMA/PDPA (◆) 0.035 wt %; $10qPDMA_{50}$-St/DPA (◇) 0.0125 wt %. The variance was typically within the size of the data points and the solid lines are a guide to the eye, rather than a fit to the data.

and PDPA homopolymers, respectively.[17] The degree of microgel character is reflected in the volumetric swelling factor, which ranges from 5 to 49. Swelling factors greater than 10 indicate good microgel character and may be compared with the swelling factor of 125 reported by Loxley and Vincent for P2VP-based microgels.[14]

Aqueous electrophoresis measurements were carried out on dilute aqueous dispersions of all microgels. In each case a sigmoidal curve was observed and the various isoelectric points are summarized in Table 1. Zeta potential vs pH curves for four representative microgels are depicted in Figure 6. The zeta potential is a shear plane measurement, and as such it is sensitive to the nature of the stabilizer chains, as well as the particle cores. The two microgels synthesized using the nonionic PEGMA stabilizer (entries 4 and 7 in Table 1) have significantly lower isoelectric points (at pH 6.8 and pH 7.6, respectively) than those observed for the two microgels prepared using the tertiary amine methacrylate-based macromonomers (entries 5 and 8 in Table 1). The PEGMA-stabilized PDPA microgel has a lower isoelectric point than the PEGMA-stabilized PDEA microgel, as expected. However, there is relatively little difference between the two isoelectric points (both around pH 9) observed for the 10qDMA-St/PDPA and the PDMA-St/PDEA microgels. This suggests that the nature of the stabilizer has a bigger influence on the isoelectric point than the nature of the core particles. This leads to an interesting observation for the PDMA-St/PDEA microgel. Comparison of the hydrodynamic diameter and zeta potential data presented in Figures 5 and 6 suggests three distinct regimes for these particles. Above pH 9, the particles are in their nonsolvated latex form and there is little or no cationic charge on the PDMA stabilizer chains, which has a pK_a of around 7.0. As the pH is reduced from pH 9 to pH 7, the stabilizer chains charge up as they become protonated, but the PDEA cores remain nonsolvated (no appreciable increase in hydrodynamic diameter). Thus the particles exist as latex particles surrounded by a cationic stabilizer layer. Below pH 7, the PDEA cores also become protonated and the latex-to-microgel swelling transition occurs. The accompanying change in physical appearance is clearly seen in Figure 3. Prior to our measurements, these three regimes (or more specifically, the intermediate regime) were not anticipated because the pK_a values of linear PDMA and PDEA homopolymers are very similar.[17] Presumably, the well-solvated PDMA stabilizer chains are somewhat easier to protonate than the nonsolvated PDEA latex cores.

The zeta potential behavior of the $10qPDMA_{50}$-St/PDEA microgel (entry 6 in Table 1) is also interesting. Despite its stabilizer content of 6.1%, the IEP is similar to that of the PEGMA-stabilized PDEA microgel. However, the former microgel has a more negative zeta potential at high pH, which is more similar to the behavior of the SDS/PDEA microgel (data not shown). This suggests that the surface layer of grafted $10qPDMA_{50}$-St chains may be "patchy", possibly because not all the stabilizer is located at the particle surface. This hypothesis is supported by the observation of a region of colloidal instability between pH 6.7 and pH 7.6 for this latter microgel.

Swelling Kinetics for the Latex-to-Microgel Transition. There are a number of studies of the kinetics of swelling of microgels[10,14] and gels.[24] The most pertinent paper to the present work is that by Loxley and Vincent, who monitored the kinetics of swelling of pH-responsive P2VP-based microgels using stopped-flow apparatus to ensure rapid mixing of the microgel with the added acid.[14] It was found that higher levels of cross-linker led to slower microgel swelling, as expected. Time scales for complete swelling were typically of the order of 30 s. In view of this, we felt that stopped-flow techniques were probably unnecessary and conventional turbidimetry studies would suffice. Typical turbidimetric data are shown in Figure 7. The acid-induced latex-to-microgel transition was complete within 12 s for all microgels listed in Table 1. This is somewhat faster than that reported by Loxley and Vincent for P2VP microgels.[14] It is clear from Figure 7 that the more hydrophobic PDPA-based microgels swell more slowly than the PDEA-based microgels. This observation appears to be consistent with those made by Loxley and Vincent, who found that the incorporation of a hydrophobic monomer (styrene) reduced the rate of swelling of the P2VP microgels.[14] Returning to the present study, an increase in the background electrolyte concentration reduces both the microgel swelling rate and also the extent of swelling, as shown for the $PDMA_{50}$-St/PDEA microgel. The reduced swelling is attributed to increased

(24) Tanaka, T.; Fillmore, D. J. *J. Chem. Phys.* **1979**, *70* 1214.

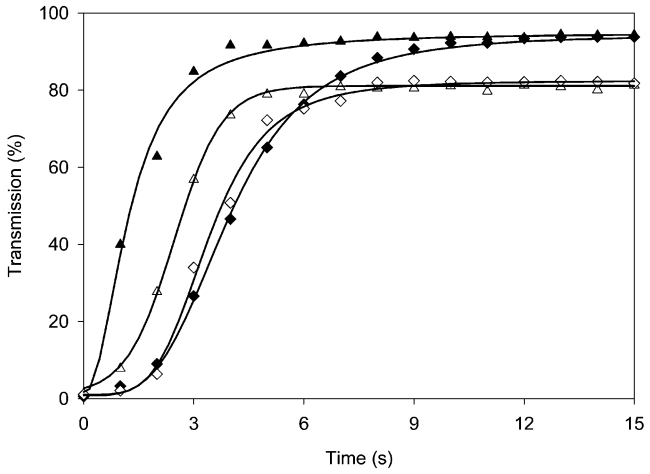

Figure 7. Kinetic studies of the latex-to-microgel swelling transition: $PDMA_{50}$-St/PDEA (▲); PEGMA/PDPA (◆); 10qP-DMA_{50}-St/PDPA (◇); $PDMA_{50}$-St/PDEA in 0.1 M NaCl (△). Conditions: transmittance wavelength was 500 nm; 0.05 wt % microgel dispersions in 0.01 M NaCl unless otherwise specified.

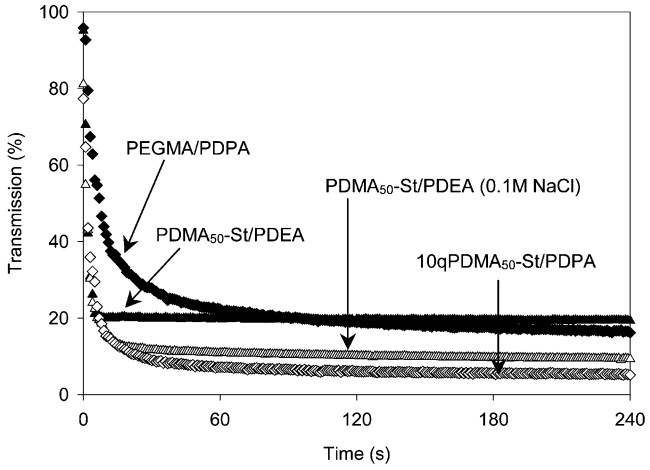

Figure 8. Kinetic studies of the microgel-to-latex deswelling transition (the final transmittance after 16 h at 20 °C, T_{16h}, is indicated after the symbols): $PDMA_{50}$-St/PDEA (▲), T_{16h} = 15.5%; PEGMA/PDPA (◆), T_{16h} = 1.6%; 10qPDMA_{50}-St/PDPA (◇), T_{16h} = 1.3%; $PDMA_{50}$-St/PDEA in 0.1 M NaCl (△), T_{16h} = 5.9%. Conditions: transmittance wavelength was 500 nm; 0.05 wt % microgel dispersions in 0.01 M NaCl unless otherwise specified.

screening of the electrostatic repulsion between the cationic polymer chains. This effect has been noted by Saunders and Vincent[22] for anionic microgels and can also be viewed as a net reduction in the osmotic pressure difference between the interior of the swollen microgel particles and the bulk solution. Tanaka and Fillmore[24] suggested that gels of submicrometer dimensions should swell to their maximum size on a millisecond time scale. However, studies by Loxley and Vincent[14] indicate that this hypothesis may not hold for relatively small microgels. Indeed, there is no evidence in the present work for the simple relationship between the swelling rate and the linear gel dimension predicted by Tanaka and Fillmore.[24]

Deswelling Kinetics for the Microgel-to-Latex Transition. The diffusion of hydroxide anions into the cationic microgel particles and the subsequent neutralization of the protonated amine residues should both occur rapidly. Thus we had originally expected to observe rapid deswelling of the swollen microgels. However, our turbidimetric studies (see Figures 7 and 8) show pronounced hysteresis effects. Initially, the rate of deswelling appears to be almost as rapid as that of swelling, but *complete* deswelling (i.e., recovery of the original transmittance) requires time scales of many hours at 20 °C. These observations can be rationalized as follows. For microgel contraction to occur, both its water content and also the salt generated during neutralization must be excreted. Contraction occurs initially, since the polymer chains are rapidly deprotonated and therefore no longer cationic. However, this contraction necessarily leads to an increase in the local salt concentration within the microgel, which in turn causes water from the bulk solution to enter the microgel in order to lower the local salt concentration. It is this ingress of water due to the increase in osmotic pressure that retards the rate of microgel deswelling in its latter stages. In principle, if the salt concentration in the bulk solution were increased so that it was higher than the local salt concentration within the swollen microgel (estimated to be 0.1−0.3 M, depending on the volumetric swelling factor of the microgel), no hysteresis would be observed. However, this relatively high background salt concentration usually caused coagulation once the particles return to their nonsolvated latex form. Clearly, such hysteresis effects do not occur in the deswelling of thermoresponsive PNIPAM-type microgels, since there is no buildup of salt within the microgel interior in this case.

Applications for these new film-forming microgels are currently being evaluated in our laboratory. For example, in situ atomic force microscopy studies of surface-adsorbed microgels are in progress and will be reported in due course. In this context it is worth emphasizing that the 10qPDMA-St/PDEA microgel has a very similar chemical structure to the partially quaternized PDMA-PDEA diblock copolymer micelles recently reported by Webber and co-workers.[25] In these micelle studies the degree of quaternization on the coronal PDMA block had a profound influence on the nature and behavior of the adsorbed micellar layer; similar effects might be achieved for the analogous microgels by varying the nature of the steric stabilizer. Moreover, microgels are much more conveniently synthesized than block copolymers, produce thicker adsorbed overlayers, and have much greater capacities for the loading and release of hydrophobic actives (drugs, pesticides, fragrances, etc.).

Conclusions

A new class of lightly cross-linked pH-responsive microgels based on either 2-(diethylamino)ethyl methacrylate or 2-(diisopropylamino)ethyl methacrylate has been synthesized by emulsion polymerization at pH 8−9 using either small molecule surfactants or various well-defined macromonomer stabilizers. Mean particle diameters ranged from 250 to 700 nm, depending on the synthesis conditions. Unlike the high T_g poly(vinylpyridine)-based microgels reported previously, the 2-(diethylamino)ethyl methacrylate-based microgels were soft and film forming; moreover, the latex-to-microgel transition was observed at around neutral pH. The 2-(diisopropylamino)ethyl methacrylate-based microgels exhibited qualitatively similar behavior, but swelling occurred at a lower pH due to the increased hydrophobicity. DLS measurements indicated that swelling was reversible for both types of microgels, and ^{1}H NMR studies confirmed that protonation of the tertiary amine groups occurred at low pH,

(25) (a) Webber, G. B.; Wanless, E. J.; Bütün V.; Armes, S. P.; Biggs, S.; *Nano Lett.* **2002**, *2*, 1307. (b) Webber, G. B.; Wanless, E. J.; Armes, S. P.; Biggs, S. *Faraday Discuss.* **2004**, *128*, in press.

as expected. Aqueous electrophoresis studies corroborate this hypothesis: microgels synthesized using nonionic macromonomer stabilizers exhibited isoelectric points that corresponded approximately to the known pK_a values of the respective DEA and DPA homopolymers. In contrast, use of amine-based macromonomers led to isoelectric points being observed at higher pH. The latex-to-microgel transition occurred rapidly, but microgel deswelling required many hours for complete recovery, indicating significant hysteresis effects. This is believed to be due to the excretion of electrolyte from the microgel interior being retarded by the ingress of water due to substantial differences in osmotic pressure between the microgel interior and the bulk solution. Applications for these new film-forming microgels are currently being evaluated in our laboratory. For example, in situ atomic force microscopy studies of surface-adsorbed microgels are in progress and will be reported in due course.

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Note Added in Proof. A closely related paper by Y. Nagasaki and co-workers on pH-responsive "nanogels" appeared in Macromolecules after submission of the present manuscript. See Hayashi, H.; Iijima, M.; Kataoka, K.; Nagasaki, Y. *Macromolecules* **2004**, *37*, 5389.

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