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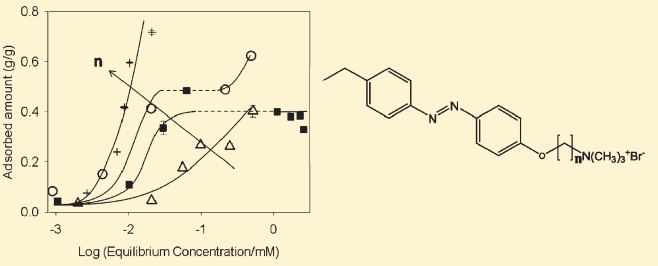
Effect of Chain Length on the Interaction between Modified Organic Salts Containing Hydrocarbon Chains and Poly(*N*-isopropylacrylamide-*co*-acrylic acid) Microgel Particles

Kaizhong Fan, Melanie Bradley,* Brian Vincent, and Charl F. J. Faul

School of Chemistry, University of Bristol, Bristol BS8 1TS, U.K.

Supporting Information

ABSTRACT: A series of four hydrophobically modified, diphenylazo-based organic salts have been prepared and characterized. To achieve this a C_x (x = 4, 6, 8, or 10) hydrocarbon chain was inserted between the diphenylazo moiety and the quaternary ammonium headgroup of the salt. The absorption of each of the four modified organic salts into anionic microgel particles of poly(*N*-isopropylacrylamide-*co*-acrylic acid) has been studied at pH 8. In addition, the hydrodynamic diameters and electrophoretic mobilities of the microgel particles have been studied as a function of the organic salt concentration, also at pH 8. In addition to the electrostatic attraction between the quaternary ammonium head groups of the organic salts and the anionic groups within the microgel particles, hydrophobic association between the chains of the organic salts within the microgel particles plays a role, with this effect increasing strongly from x = 4 to 10. Desorption of the x = 4 and 6 organic salts occurs readily on changing, in situ, the pH from 8 to 2.5 (and thereby eliminating the electrostatic interaction) but is only partially achieved for the x = 8 and 10 organic salts. Indeed, for the x = 10 organic salt, only about 80% of the organic salt is desorbed upon dilution of the microgel particles into a large excess of water.



INTRODUCTION

Microgel particles have been widely studied in recent years,[1] both with regard to understanding their physical properties and also in exploiting their potential applications, for example, in drug delivery,[2,3] as biosensors,[4,5] and in surface coatings.[6] An important feature of microgel particles is their stimulus-responsive behavior, in particular they may change their size in response to external triggers such as changes in temperature,[7−9] pH,[10−13] or solvency.[14,15] When microgel particles are in their swollen state, they may absorb molecules, or even nanoparticles, provided there is some attraction between the adsorbate and the cross-linked polymer network of the microgel particles.

In a recent paper[16] we reported on the absorption of organic salts (OS), containing one, two, or three sulfonate groups, into cationic poly(vinylpyridine) (PVP) microgel particles at pH 3, where the pyridine moieties are fully protonated. The structures of these three OS's are shown in Figure 1.

The principle adsorption mechanism was found to be an electrostatic one, with the adsorbed amount, at a given OS concentration, increasing, as might be expected, with the number of sulfonate groups per OS molecule. The adsorption isotherms, however, were all low affinity. Moreover, for each of the OS molecules studied there was a limiting concentration, beyond which the PVP microgel particles aggregated. This was attributed to the observed decrease in size of the microgel particles, with increasing OS molecule absorption. A decrease in size of the microgel particles leads to an increase in the net Hamaker constant of the particles, as water is excluded from their interior. At the point where aggregation occurred with each of the three OS molecules, the diameter of the microgel particles had been reduced from about 1200 nm, in the absence of added OS molecules (and pH 3), to around 200 nm. At this size the van der Waals attraction between the microgel particles is sufficient to overcome any residual electrostatic repulsion between them, leading to the observed particle aggregation. The calculated ratio of absorbed OS molecules per pyridine moiety at the onset of aggregation was significantly less than 1 (the greatest value being ~ 0.4 for the OS molecules with only one sulfonate group). Moreover, no reversal of charge of the microgel particles could be achieved by increasing the added OS concentration. If reversal of charge had occurred, then the microgel particles should have reswollen and restabilized, allowing greater amounts of OS molecule absorption. So the low maximum absorbed amounts of OS molecules, taken together with the fact that they are only weakly absorbed and are hence likely to desorb on dilution of the microgel particles, meant that using normal OS molecules of this type in any potential applications would be severely limited.

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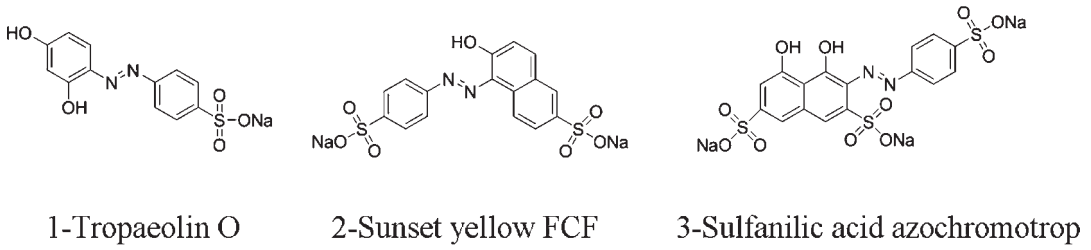

Figure 1. Organic salts used in a previous paper.[16]

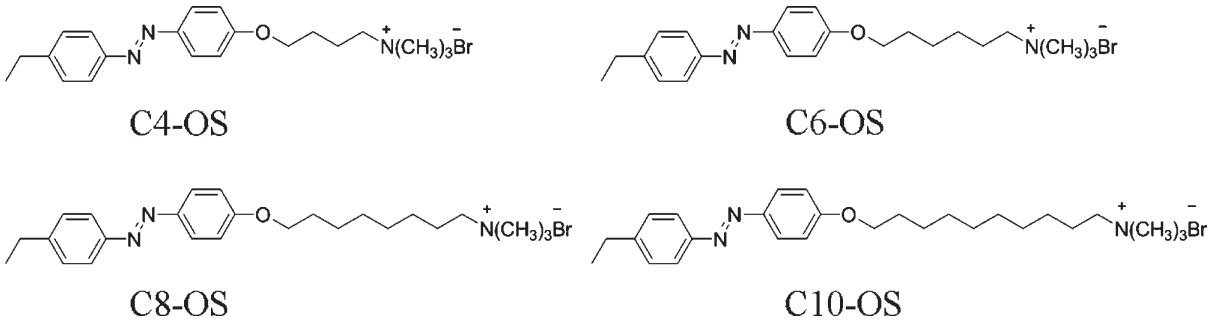

Figure 2. Hydrocarbon-modified OS's used in the present work.

In order to overcome this problem, it was felt that another mechanism of absorption needed to be introduced, in addition to the electrostatic one. In previous studies of the adsorption of both ionic and nonionic surfactant molecules[17−22] into microgel particles, it had been observed that hydrophobic interactions [between the hydrocarbon tails of the surfactant molecules and the hydrophobic moieties in microgel particles based on poly(NIPAM)] contributed significantly to the adsorption mechanism. In addition, when ionic surfactants of opposite charge to the microgel particles were studied, charge reversal was observed at sufficiently high added surfactant molecule concentrations, even though particle aggregation was observed over a certain, lower surfactant concentration range. It was also shown[17,18] that, in the reversed charged region, the number of adsorbed surfactant molecules per charge group in the microgel particles was very much greater than one. This suggested that some form of surfactant aggregation was occurring around each charged site of the microgel particles, as is known to occur for ionic surfactant molecules around polyelectrolyte chains of opposite charge, beyond the so-called "critical aggregation concentration" of surfactant.[23] This led us to the following strategy, i.e., to insert hydrocarbon chains as spacers between the OS molecules's hydrophobic core and charge, thus allowing the modified OS molecules to behave in a similar fashion to the more classical ionic surfactants in terms of their interaction with microgel particles containing charged groups of opposite sign. In this way, both higher absorbed amounts of the OS molecules (in the charge-reversed region) and stronger absorption might be achieved.

This concept forms the basis of the present paper. Initially we attempted to attach a hydrocarbon chain to the OS with one sulfonate group reported in our previous paper,[16] namely, *1-tropacolin-O*, the structure of which is shown in Figure 1. However, this proved to be difficult synthetically. Hence, it was decided to use a cationic version of a similar diphenylazo compound, to which the attachment of hydrocarbon chains had been successfully achieved.[24] Four such modified OS molecules, with different hydrocarbon chain lengths, were successfully synthesized, and their structures are shown in Figure 2.

These molecules could be regarded as cationic surfactants with a diphenylazo moiety attached to the end of the hydrocarbon tail. Since these hydrophobically modified OS's are cationic, it was also necessary to change the microgel particles, from the cationic PVP particles used in the previous work[16] to an anionic system. To this end, poly(*N*-isopropylacrylamide-*co*-acrylic acid) (PNIPAM-*co*-AAc) microgel particles were used. These anionic microgels have been widely studied previously.[25] They are known to be negatively charged, even under acidic conditions, if an initiator such as potassium persulfate is used in their synthesis, as this leads to the presence of strong acid groups (sulfonate) at the particle periphery. However, their overall negative charge increases strongly with increasing pH as the acrylic acid moieties within the interior of the microgel particles become increasingly ionized.

In the present paper, we present studies of the effect of the four modified OS's shown in Figure 2 on the diameter and electrophoretic mobility of the PNIPAM-*co*-AAc microgel particles at pH 8, where the microgel particles are strongly negatively charged. The corresponding adsorption isotherms have also been established for the four modified OS's at pH 8. In addition, the effects of (i) changing the pH from 8 to 2.5 (at the same particle concentration) and (ii) diluting the microgel particles with water on the adsorption isotherms have been investigated. At pH 2.5, the only anionic charge on the microgel particles comes from the surface sulfonate groups; all the AAc moieties are in the undissociated form. In this way, we are able to assess the relative strengths of the electrostatic and hydrophobic interactions between the modified OS's and the microgel particles. Furthermore, we were able to determine whether sufficiently high absorbed amounts could be achieved and whether desorption on changing pH or upon simple dilution would be effected or restricted, as desired for any particular application.

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EXPERIMENTAL SECTION

Materials. *N*-Isopropylacrylamide (NIPAM) and *N*,*N*-methylenebisacrylamide (BA) were both from Fisher. NIPAM was recrystallized from hexane. Potassium persulfate (KPS), an anionic initiator, was used as received from Sigma-Aldrich. 4-Ethylaniline (98%), sodium nitrite ($NaNO_2$) (99.5%), phenol (99%), 1,4-dibromobutane (99%), 1,6-dibromohexane (96%), 1,8-dibromooctane (98%), 1,10-dibromodecane (97%), and trimethylamine (TMA) in solution in ethanol (31−35 wt %) were all purchased from Sigma-Aldrich. Potassium iodide (KI) was purchased from BDH Chemicals. Sodium hydroxide (NaOH), sodium carbonate (Na_2CO_3), potassium carbonate (K_2CO_3), methanol, dichloromethane, and 37% hydrochloric acid (HCl) solution were all purchased from Fisher Scientific. Except where stated, all chemicals were used as supplied. Milli-Q water was used wherever needed.

Instrumentation. The NMR ^{1}H spectrum for each of the four organic salts in dimethyl sulfoxide-d_6 (DMSO-d_6) solution was determined using a JEOL ECP 400 instrument, at 20 °C.

Mass spectrometry (MS) analysis on each of the four organic salts was carried out using an Apex 4,7 T Fourier-transform ion-cyclotron resonance mass spectrometer (Bruker Daltonics, Coventry, UK), fitted with an Apollo electrospray ionization source. Samples were dissolved in a methanol/dichloromethane mixture (50:50 by vol), at a concentration of approximately 10 μg mL^{-1} and directly infused at 120 μL h^{-1} into the electrospray ionization source from a syringe pump. (These measurements were kindly carried out by the mass spectrometry facility in the School of Chemistry at the University of Bristol).

Surface tension measurements on solutions of each of the OS molecules in water were made using a Kruss K100 tensiometer, fitted with a platinum ring. Plots of surface tension (γ) against log OS concentration (c) were constructed for each OS molecule, from which the critical micelle concentration (cmc) and the area per OS molecule (a_S) at the air/solution interface could be determined.

The saturation solubility of each of the four OS molecules in water, at 20 °C, was determined as follows. For C4-OS, C6-OS, and C8-OS, 0.001 g of the organic salt was added to 1 mL of Milli-Q water. This procedure was repeated for each organic salt until some undissolved material was observed, even after stirring overnight. For C10-OS, a similar procedure was used, except that 0.001 g of the organic salt was added to 100 mL of Milli-Q water initially.

Absorption Isotherms for the Organic Salts into the Microgel Particles. Appropriate amounts of microgel dispersion, organic salt solution, and Milli-Q water, each at pH 8, were mixed to give a suitable range of initial organic salt concentrations (c^0 /M), in a total volume (V) of 10^{-2} L. The mixtures were allowed to stand for 48 h in order to equilibrate. Afterward, each dispersion was centrifuged at 10 000 rpm, at 20 °C. The supernatant was collected and analyzed using UV−vis spectroscopy. The equilibrium concentration (c^{eq}/M) of the organic salt was determined from the corresponding calibration curve.

The absorbed amount (Γ, wt/wt) of each organic salt in the microgel particles could then be calculated from eq 1

$$\Gamma = \frac{(c^0 - c^{eq})VM}{m} \quad (1)$$

where m is the mass of (dry) microgel present and M is the molar mass of the organic salt.

The change in the absorbed amount for each of the dispersions was then determined on changing the pH, in situ, from 8 to 2.5. This was achieved by reanalyzing the supernatant concentration after sufficient concentrated HCl solution had been added (in microliter quantities) to each of the (remixed) dispersions to adjust the pH to 2.5 and the dispersions had been allowed to stand for a further 48 h.

Similarly, the change in the absorbed amount for C10-OS, at one initial concentration, was determined after replacing the supernatant with water and allowing the system to stand for a given time, before centrifuging and reanalyzing the supernatant concentration. The time intervals chosen were 5, 15, 30, 45, 60 min.

Synthesis of PNIPAM-*co*-AAc Microgel Particles. NIPAM (3.2 g, 0.028 mol) and BA (0.4 g, 2.6 mmol) were added to a 500 mL reaction vessel and dissolved in 300 mL of Milli-Q water followed by addition of 15 mL of Milli-Q water solution containing AAc (0.4 g, 5.56 mmol). After purging with nitrogen for 10 min, the solution was heated to 70 ± 1 °C and stirred at 350 rpm. KPS (0.12 g, 0.44 mmol), dissolved in Milli-Q water (7 mL), was added to the reaction flask and the solution turned turbid within 5 min. The reaction was left to proceed for a further 10 h and then left to cool to room temperature. The resultant microgel particle dispersion was dialyzed against Milli-Q water to remove any low molecular weight oligomers and unreacted materials; the water was renewed each day for 7 days.

Characterization of the Microgel Particles. The diffusion coefficients of the microgel particles in water at ambient temperature were determined by photon correlation spectroscopy (PCS) using a Brookhaven Instruments Zeta Plus apparatus, fitted with a 15 mW laser (wavelength 678 nm). The Stokes−Einstein equation was used to calculate the hydrodynamic diameter of the particles from the diffusion coefficient. The electrophoretic mobility of the microgel particles in 1 mM KCl was determined by phase analysis light scattering (PALS) using the same instrument.

In order to determine the number of charge groups per microgel particle, a potentiometric titration of the acrylic acid groups in the microgel particles was carried out as follows: 10 mL of the synthesized microgel particle dispersion was diluted with 40 mL of Milli-Q water and adjusted to pH 1.92. This microgel dispersion was then titrated with a solution of 0.05 M sodium hydroxide and the equilibrium pH recorded at each stage. As a control experiment, 50 mL of Milli-Q water was adjusted to pH 1.92 and also titrated with 0.05 M sodium hydroxide solution.

Synthesis of Organic Salts. The method reported by Oakley[24] was used to synthesize the four organic salts shown in Figure 2. Three steps were involved in each preparation, as described below.

i. Preparation of 4-((4-Ethylphenyl)diazenyl)phenol. Three solutions were prepared as follows: (A) 4-ethylaniline (24.2 g, 0.2 mol) was dissolved in of a mixture of 250 mL of acetone and 250 mL of Milli-Q water containing 20 mL of HCl solution (37%). The solution was stirred for 20 min in an ice bath. (B) $NaNO_2$ (13.8 g, 0.2 mol) was dissolved in 200 mL of distilled water and placed in a freezer to cool to 1−3 °C. (C) Phenol (18.8 g, 0.2 mol), NaOH (8 g, 0.4 mol), and Na_2CO_3 (21.2 g, 0.2 mol) were dissolved in 200 mL of Milli-Q water, stirred for 5 min, and then also placed in the freezer to cool to 1−3 °C. Once the solutions had cooled, solution B was slowly added to solution A and left for 20 min to stir in an ice bath. The diazonium salt solution generated by mixing solutions A and B was added drop by drop to the phenol solution (solution C), ensuring at all times the reaction temperature did not exceed 8 °C. The yellow/brown precipitate was filtered off and dried overnight in a vacuum oven. The crude product was recrystallized from ethanol, producing a yellow powder.

ii. Preparation of Bromoalkylated 4-((4-Ethylphenyl)diazenyl) phenol. The product from step i was used to react with 1,4-dibromobutane, 1,6-dibromohexane, 1,8-dibromooctane, or 1,10-dibromodecane. Only the reaction with 1,4-dibromobutane is described here. 4-((4-Ethylphenyl)diazenyl)phenol (4.5 g, 0.02 mol) was dissolved in 100 mL of acetone. 1,4-Dibromobutane (21.6 g, 0.1 mol), anhydrous K_2CO_3 (7 g, 0.05 mol), and KI (0.1328 g, 0.8 mmol) were all dissolved in 100 mL of acetone and then added to the previous solution. The reaction mixture was refluxed at 75 °C and stirred for 20 h. The solution was then allowed to cool to room temperature, after which the acetone was removed by rotary evaporation. The resulting precipitate was washed with 50 mL of hexane in a Buchner funnel connected to a vacuum pump.

Table 1. Molecular Mass (M), Critical Micelle Concentration (cmc) in Water, Area per OS Molecule at the Air/Water Interface (a_S), and the Saturation Solubility (S) in Water, for Each of the OS Molecules[a]

	M (g mol^{-1})				
OS	calcd, without Br^-	expl, from MS	cmc (mM)	a_S (nm^2)	S (mM)
C4-OS	340	340	3.9	0.65	114
C6-OS	368	368	1.3	0.71	56
C8-OS	396	396	0.66	1.3	19
C10-OS	424	424	0.07	2.8	0.18

[a] Note that mass spectra (MS) are provided in the Supporting Information.

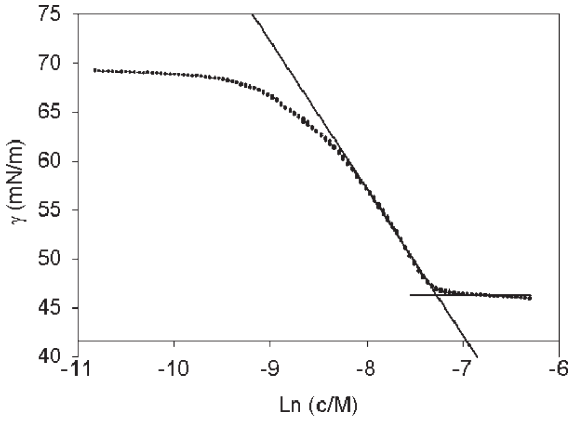

Figure 3. Surface tension (γ) against ln (c/M) for surfactant C8-OS at 20 °C.

Then the product was washed with 50 mL of Mili-Q water several times before being dried in a vacuum oven overnight. The precipitate was recrystallized from ethyl acetate twice.

iii. Preparation of Cationic Organic Salts. The product from step ii (1 g, 2.77 mmol) was dissolved in 100 mL of toluene in a round-bottom flask. Trimethylamine solution in ethanol (10 mL, 42 mM) was added and the solution was refluxed at 90 °C for 24 h. The solution was allowed to cool to room temperature, and then the solvent was removed by using a rotary evaporator. The resultant solid was purified by dissolving the precipitate in toluene and centrifuging the solution at 10 000 rpm for 20 min, retaining the solid. This process was repeated until the toluene phase was not colored. The solid was then recrystallized from ethanol. The purified solid was then dried in a vacuum oven overnight. The purity of the product was confirmed by ^{1}H NMR, for C4-OS: (300 MHz, DMSO-d_6, 21 °C, TMS) δ = 1.22 (t, 3H, CH_3), 1.74−1.90 (m, 4H, $2CH_2$), 2.64−2.75 (m, 2H, CH_2), 3.03−3.12 (s, 9H, $3CH_3$), 3.38−3.44 (m, 2H, CH_2), 4.11−4.18 (t, 2H, CH_2), 7.12−7.18 (d, 2H, 2CH), 7.37−7.44 (d, 2H, 2CH), 7.72−7.81 (d, 2H, 2CH), 7.85−7.92 (d, 2H, 2CH).

C6-OS, C8-OS, and C10-OS were all prepared following the same procedure. The ^{1}H NMR results and sample spectra are provided in the Supporting Information.

RESULTS AND DISCUSSION

Characterization of the Organic Salts. The MS results (Table 1) show that the desired OS molecules were prepared successfully. These results were confirmed by the ^{1}H NMR results.

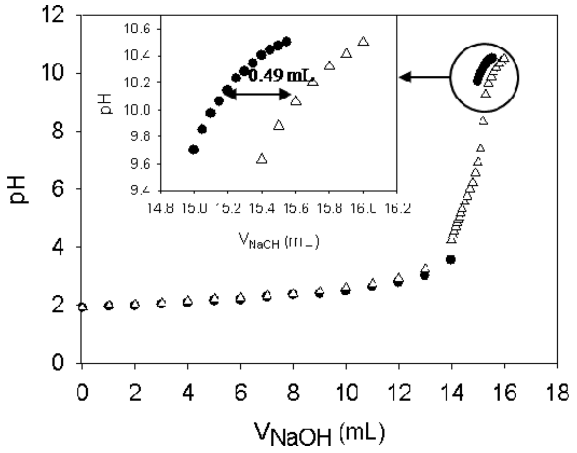

Figure 4. Potentiometric titration of the microgel particles (△) and Milli-Q water (●): pH against volume of 0.05 M NaOH added.

The surface tension (γ) versus ln c plot for C8-OS is shown in Figure 3. Similar plots were obtained for the other three organic salts. The cmc value was taken as the concentration where the two straight lines shown in Figure 3 intersect. The cmc values decrease with increasing hydrocarbon chain length, as expected (Table 1). For C4-OS and C6-OS, the cmc value reduces by a factor of ∼2 on adding two further carbon atoms. However, a much bigger decrease (a factor of ∼9) occurs on going from C8-OS to C10-OS. A similar disparity is seen in the solubility (S) values given in Table 1. Clearly, adding the two extra carbon atoms in going from C8-OS to C10-OS increases the hydrophobicity of the molecule considerably.

The a_S value was obtained as follows. The maximum value of the gradient of the curve [dγ/d(ln c)], just prior to the cmc (see Figure 3), was first determined. The Gibbs equation (eq 2) was then used to calculate the maximum adsorbed amount (Γ_{max}^{aw}) of the OS molecule at the air/solution interface.

$$\Gamma_{max}^{aw} = \frac{1}{2RT}\left(\frac{d\gamma}{d(\ln c)}\right) \quad (2)$$

where R is the gas constant and T the absolute temperature. The factor "2" in the denominator is to account for the fact that the organic salts dissociate into two ions.

By assuming that the maximum adsorbed amount corresponds to a close-packed monolayer of OS molecules at the air/solution interface, the value of a_S may be obtained from eq 3

$$a_S = \frac{1}{\Gamma_{max}^{aw} N_A} \quad (3)$$

where N_A is Avogadro's number. a_S for a close-packed monolayer of linear hydrocarbon chains, oriented normal to the air/water interface, is ∼0.2−0.6 nm^2.[26] The values for the organic salt cations, listed in Table 1, are somewhat greater, as is to be expected, since both the quaternary ammonium headgroups and the hydrophobic tails are rather bulky. Thus, the value of 0.65 nm^2 seems quite reasonable for C4-OS. It is interesting that the a_S values increase with increasing hydrocarbon chain length in the series C4-OS to C10-OS, with the value increasing by a factor of ∼2 in going from C8-OS to C10-OS. The reason for this is not obvious. It may be that, because of the more complex structure of the hydrophobic tails of these organic salts compared to more conventional surfactant molecules with

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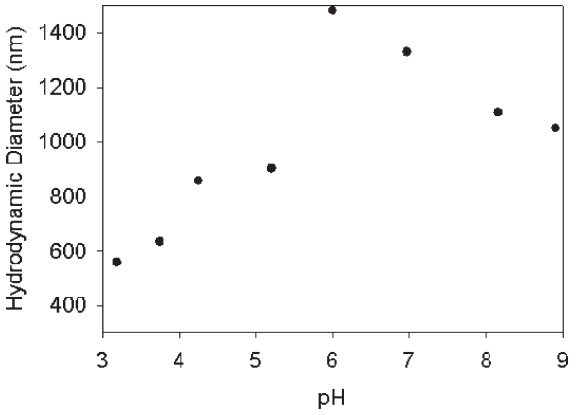

Figure 5. Hydrodynamic diameter of the microgel particles as function of pH, at 20 °C.

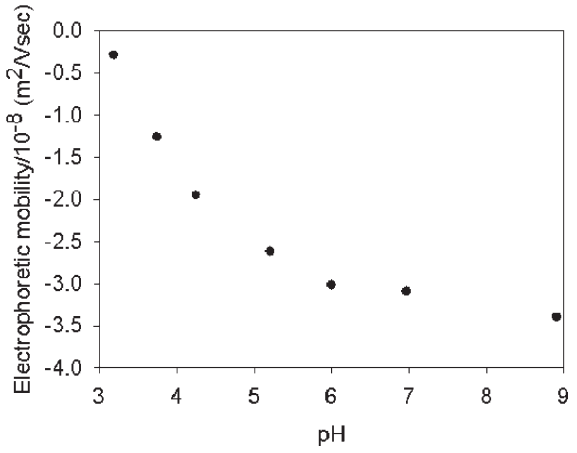

Figure 6. Electrophoretic mobility of the microgel particles as a function of pH in a background concentration of KCl of 1 mM.

straight-chain hydrocarbon tails, the packing of the C10-OS tails in the micelles and at the air/water interface is substantially different, so that the cmc is reached well before maximum adsorption at the air/water interface is attained.

Characterization of the Microgel Particles. *Concentration of Carboxylic Acid Groups in the Microgel Dispersion.* The potentiometric titration of the microgel dispersion (at the same particle number concentration as used in the organic salt absorption experiments to be discussed later) and that for Milli-Q water are shown in Figure 4. The difference (0.49 mL) in the volumes of added NaOH solution required to obtain the same pH change for the microgel dispersion and for water is reasonably constant when the pH is above 9.7. The concentration of carboxylic acid groups in the stock microgel dispersion is calculated to be 0.000 49 mmol mL^{-1}. This figure may be compared with the concentration of carboxylic acid groups in the stock microgel dispersion calculated from the amount of acrylic acid used in the preparation of the microgel particles, namely, 0.0011 mmol mL^{-1}. Thus, only ∼45% of the acrylic acid is actually incorporated into the microgel particles. The rest is presumably present, after the preparation, as free (poly)acrylic acid, which is then dialyzed out of the dispersion during cleanup.

Figure 5 shows the hydrodynamic diameter of the PNIPAM-*co*-AAc microgel particles as a function of pH. It can be seen that

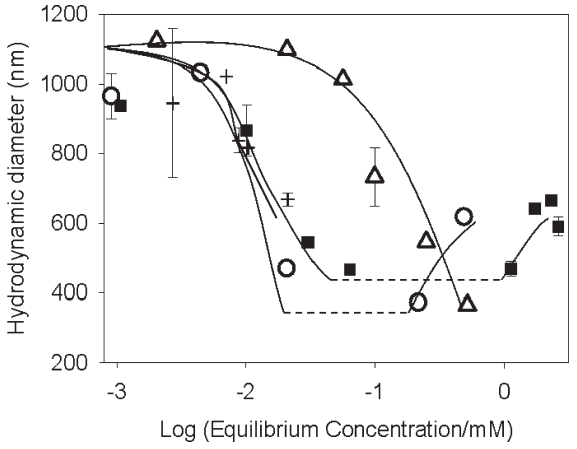

Figure 7. Hydrodynamic diameter of the microgel particles as a function of equilibrium concentration (on a log scale, for clarification) at pH 8 and 20 °C: (△) C4-OS, (■) C6-OS, (○) C8-OS, (+) C10-OS. The lines are for guiding the eye only. (---) OS concentration regions where measurements could not be made due to flocculation of the microgel particles.

over the pH range from ∼3 to ∼6, the diameter increases; this osmotic swelling is due to dissociation of the −COOH groups in the acrylic acid moieties with increasing pH and the resultant uptake of counterions (Na^+ ions from the added NaOH) into the microgel particle interior. Beyond pH ∼ 6, the hydrodynamic diameter decreases again; this is due to the systematic increase in the background electrolyte concentration in solution, resulting from the incremental addition of NaOH to increase the pH.

Diameter of the Microgel Particles as a Function of pH. Figure 6 shows the electrophoretic mobility of the PNIPAM-*co*-AAc microgel particles as a function of pH, in a background KCl concentration of 1 mmol L^{-1}. As expected, the magnitude of the (negative) electrophoretic mobility increases over the pH range ∼3 to ∼9, again due to the increasing dissociation of the −COOH groups in the interior of the microgel particles. At pH 3, where the −COOH groups are almost entirely in the *undissociated* form, the small, negative electrophoretic mobility value arises from the initiator residues (sulfonate groups) at the periphery of the particles, which are formed during the polymerization process used to prepare the microgel particles.

Hydrodynamic Diameter of the Microgel Particles as a Function of Added OS Concentration, pH 8. Figure 7 shows the variation in the hydrodynamic diameter (d) of the microgel particles, as a function of added OS concentration (c, on a log scale for clarity), at pH 8, for each of the four OS molecules. From Figure 5, it can be seen that the value of d for the microgel particles at pH 8, in the *absence* of any added OS, is ∼1100 nm. Upon adding the OS molecules the value of d decreases as a result of the uptake of OS cations into the interior of the anionic microgel particles. For C6-OS and C8-OS it should be noted that, with increasing concentration, there is a region of c values where the microgel particles flocculate, making the determination of their size by PCS impossible. These regions are indicated by the dashed curves in Figure 7. It is of interest that, beyond these regions where flocculation is observed, the particles become restabilized. As will be confirmed in the next section, in this restabilization region (for C6-OS and C8-OS) the microgels particles change their sign and become net *cationic*. For the C4-OS cations, flocculation occurred at concentrations

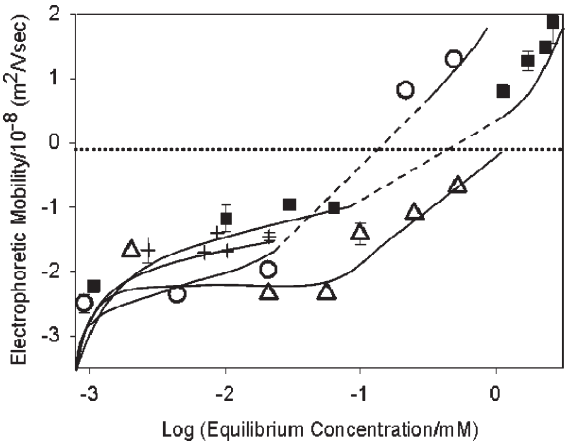

Figure 8. Electrophoretic mobility of the microgel particles as a function of equilibrium concentration (on a log scale, for clarification) at pH 8 and 20 °C: (△) C4-OS, (■) C6-OS, (○) C8-OS, (+) C10-OS. The lines are for guiding the eye only. (---) OS concentration regions where measurements could not be made since the microgel particles flocculated.

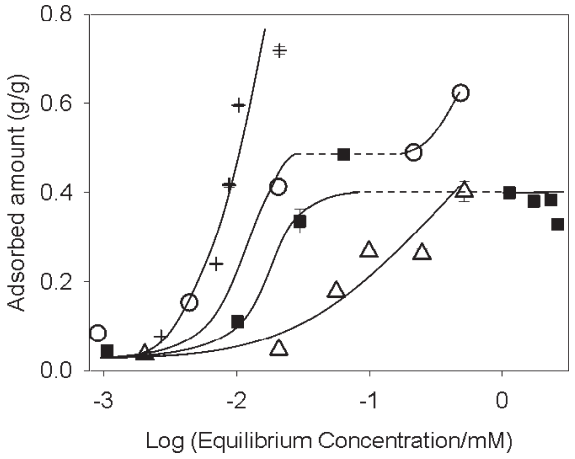

Figure 9. Adsorbed amounts as a function of equilibrium concentration (on a log scale, for clarification) at pH 8 and 20 °C: (△) C4-OS, (■) C6-OS, (○) C8-OS, (+) C10-OS. The lines are for guiding the eye only. (---) OS concentration regions where measurements could not be made since the microgel particles flocculated.

beyond the highest concentration investigated, and restabilization did not occur on increasing this concentration to higher values, up to the solubility limit. For the C10-OS cations, the range of concentrations available is limited by the very low solubility of the C10-OS molecules in water; indeed, insufficient C10-OS could be added even to reach the flocculation region.

At any given value of *c*, at least in the higher concentration range, the value of *d* decreases in the order C8 > C6 > C4. Clearly, this would suggest that the longer the carbon chain length, the greater the interaction of the OS cations with the anionic microgel particles. This would imply that there is a significant hydrophobic contribution to this interaction, in addition to the electrostatic interaction. This hydrophobic contribution becomes stronger with increasing carbon chain length. The fact that addition of sufficient C4-OS leads to flocculation, but not restabilization, even at the highest concentrations possible, suggests only a rather weak hydrophobic contribution in this case. In this regard, C4-OS behaves rather similarly to the unmodified, *anionic* OS, 1-trapaeolin-O, shown in Figure 1, whose interaction with *cationic* microgel particles was discussed in our previous paper.[16] There it was shown that the absorption of this OS molecule into the microgel particles was very weak and also that flocculation (but no restabilization) of the microgel particles occurred at sufficiently high concentrations of the OS molecule. Hence, it would seem that insertion of a C4 carbon chain is insufficient to introduce significant hydrophobicity to the OS molecule.

One would predict that insertion of a C10 carbon chain should increase the hydrophobicity of the OS molecules considerably. However, the additional CH_2 units increase the hydrophbicity to such an extent so that the range of *c* values available for C10-OS is much smaller, because of its much more limited solubility in water (see Table 1). Hence, studies on the effect of this OS molecule on the hydrodynamic diameter of the microgel particles were limited to the low *c* value range (see Figure 7). In this range the effect of the added OS molecules is much less pronounced, and no distinct trends with carbon chain length may be distinguished, except that **C4-OS** has, as expected, a much weaker effect than C6-OS, C8-OS, or C10-OS.

Electrophoretic Mobility of the Microgel Particles as a Function of Added OS Concentration, pH 8. The electrophoretic mobility (u) of the microgel particles, at pH 8, in the *absence* of added OS molecules is -3.2×10^{-8} m^2 V^{-1} s^{-1}, in a background concentration of KCl of 1 mM (see Figure 6). The results obtained for u as a function of c (again on a log scale), at pH 8, for each of the four OS molecules are shown in Figure 8. The mobility data points shown in Figure 8 do not appear to extrapolate back to the value of -3.2×10^{-8} m^2 V^{-1} s^{-1} in 1 mM KCl in the *absence* of added OS molecules, presumably because the addition of the organic salts at concentrations greater than 1 mM increases the ionic strength of the solution further. The results shown in Figure 8 broadly reflect the observations reported in the previous section concerning the dependence of *d* on *c*, at pH 8 (Figure 7). First, only with the C6-OS and C8-OS molecules could the net sign of the microgel particles be reversed at sufficiently high *c* values, i.e., beyond a region of *c* where flocculation occurred (indicated by the dashed line in Figure 8); this reversal of sign occurs at a lower value of *c* for C8-OS than for C6-OS. Second, C4-OS has the weakest effect on *u*; beyond the highest range of *c* values reported here for C4-OS flocculation occurs. Third, C10-OS does not reverse the charge, because the range of *c* values that could be studied is limited by the low solubility of C10-OS in water.

Absorption Isotherms for the OS Molecules in the Microgel Particles at pH 8. The absorption isotherms for the four OS molecules in the microgel particles at pH 8 are shown in Figure 9 (again with *c* on a log scale). The dashed lines again indicate concentration regions (for the C6-OS and C8-OS molecules) where measurements could not be made because the microgel particles flocculated. In general, the absorption affinity increases in the order C10-OS > C8-OS > C6-OS > C4-OS. This again reflects the increase in hydrophobicity of the OS molecules. The hydrocarbon moieties in the OS molecules may interact with the isopropyl moieties in the NIPAM units of the microgel particles. However, it is also likely that the OS molecules behave in a similar fashion to traditional cationic surfactant molecules, in that aggregates form around the anionic $-COO^-$ groups inside the microgel particles. Such aggregation has been postulated in a previous publication from this group[25] for the absorption of

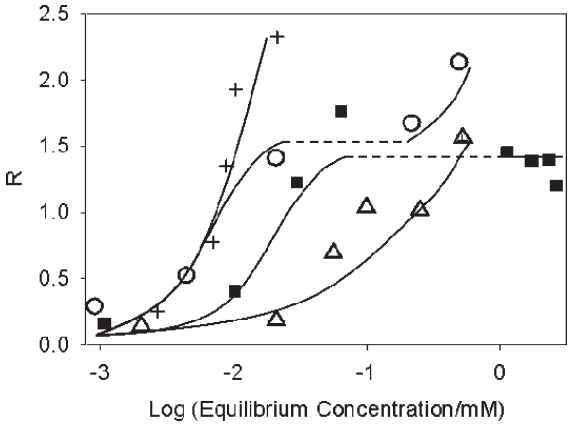

Figure 10. The number (R) of absorbed OS molecules per carboxylic acid site in the microgel particles, as a function of equilibrium concentration (on a log scale, for clarification) at pH 8 and 20 °C: (△) C4-OS, (■) C6-OS, (○) C8-OS, (+) C10-OS. The lines are for guiding the eye only. (---) OS concentration regions where measurements could not be made since the microgel particles flocculated.

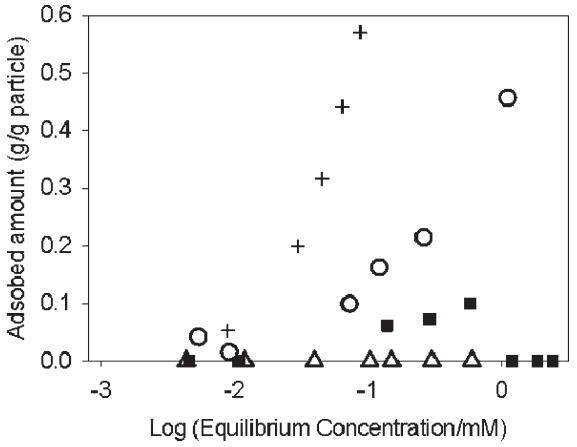

Figure 11. Adsorbed amounts as a function of equilibrium concentration (on a log scale, for clarification) at pH 2.5 and 20 °C: (△) C4-OS, (■) C6-OS, (○) C8-OS, (+) C10-OS. The lines are for guiding the eye only.

cetyltrimethylammonium chloride molecules into PNIPAM-*co*-AAc microgel particles. The exact structure of the aggregates formed within the interior of the microgel particles is not yet known, but clearly, although similar, they cannot be identical to the micelles which form in free aqueous solution above the cmc. It is quite likely with the OS molecules that any aggregates that form involve associations between the whole tail regions, i.e., the hydrocarbon units plus the diphenylazo units (see Figure 2).

In order to investigate whether more than one OS molecule is associated with each $-COO^-$ group inside the microgel particles, the absorption values have been converted from the g/g values shown in Figure 9 to the number (R) of absorbed OS molecules per anionic group in the microgel particles. The corresponding absorption isotherms plotted in this form are shown in Figure 10. In our previous study[16] of organic salt *anions* (which had not been hydrophobically modified as in the present study) absorbing into *cationic* microgel particles we found that the maximum value of R that could be achieved was 0.45. It is clear from Figure 10 that much higher values of R (>1) can be achieved with the current hydrophobically modified organic salts. This is consistent with the information gained from the hydrodynamic diameter (Figure 7) and electrophoretic mobility (Figure 8) results reported above, which showed that, at least with C6-OS and C8-OS, reversal of charge can be obtained at sufficiently high organic salt concentrations.

C6-OS is the only organic salt for which the maximum in the adsorbed amount seems to have been reached within the range of concentrations studied. For this organic salt the limiting value of R reached is slightly greater than 1, implying charge reversal at the highest concentrations studied, which is consistent with the electrophoretic mobility measurements (Figure 8). C4-OS also reaches a value of $R \sim 1$ within the concentration range studied. It is interesting that with C8-OS and C10-OS values of R much greater than 1 are achieved. Moreover, at the highest concentrations studied the absorbed amount (Figure 9) and, hence, also R (Figure 10) seem to be rising steeply still. However, it should be remembered that the value for R, determined in the way described, is only an *average* value for each microgel particle. It is highly likely that some form of organic salt association occurs around each anionic site in the microgels particles, in particular, for the organic salts with the longer hydrocarbon chains inserted. So there may well be within each microgel particle a distribution of R values, with some anionic sites having no associated organic salts located there and others a high R value locally (i.e., corresponding to the maximum number of organic salt cations associated with each anionic site, i.e., the aggregation number). Clearly the adsorbed amount would not reach a limit for C8-OS and C10-OS until all the anionic sites in the microgel particles had reached this maximum value of R. The fact that for C10-OS, at the highest concentration studied, the average value for R is 2.4 (i.e., significantly greater than 1) but no charge reversal is observed (Figure 8) is consistent with the above discussion. It may well be that the anionic sites having no associated organic salt, at this highest concentration studied, are situated more to the periphery of the microgel particles, so that the particles appear to retain their negative electrophoretic mobility at this concentration.

Absorption Isotherms for the OS Molecules in the Microgel Particles after Readjusting the pH from 8 to 2.5. Figure 11 shows the revised absorption values after changing the pH from 8 to 2.5, without changing the particle concentration. At pH 2.5 virtually all the $-COOH$ groups within the microgel particles are in the undissociated form, so the electrostatic interactions between the OS molecules and the microgel particles have been eliminated. Only the hydrophobic interactions remain. In the case of the C4-OS and C6-OS molecules, virtually all the organic salt molecules appear to have been desorbed, reflecting the very weak nature of the hydrophobic contributions in these two cases. For C8-OS and C10-OS, on the other hand, complete desorption is not achieved. For example, for C10-OS, adjustment of the pH from 8 to 2.5 leads to the following re-equilibration: at pH 8 the adsorbed amount is 0.72 g/g at 0.02 mM; at pH 2.5 this becomes 0.57 g/g now at a raised concentration in solution of 0.06 mM (i.e., just below the cmc value of 0.07 mM; see Table 1).

For both C8-OS and C10-OS, it is clear that hydrophobic association of the cationic tails is occurring within the microgel particles, in the absence of any electrostatic attraction. This is consistent with the discussion in the last section in regard to the R values achieved with these two organic salts. It is also known from previous work[21] that *nonionic surfactants* are absorbed by PNIPAM-*co*-AAc microgel particles, and it was suggested in that

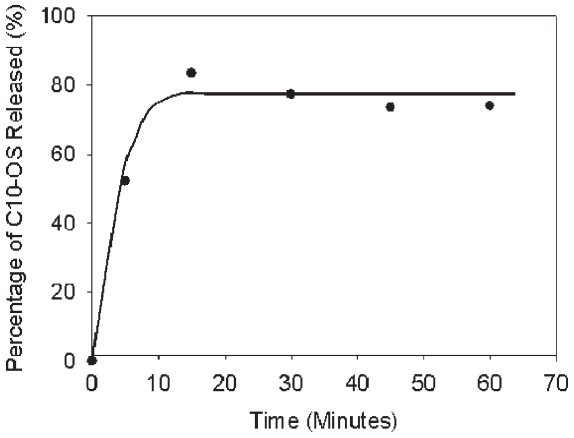

Figure 12. Desorption of C10-OS from the microgel particles, at an initial equilibrium concentration of 0.02 mM and pH 8, on replacing the supernatant with water and allowing the system to re-equilibrate for different times prior to analysis of the new supernatant concentration. The line is a guide to the eye.

work that some form of hydrophobically driven surfactant aggregation process occurs within the microgel particles.

Desorption of the OS Molecules from the Microgel Particles after Dilution with Pure Water. In order to establish whether complete desorption occurs when the system is diluted with a large excess of pure water, the following experiment was carried out with the C10-OS organic salt (this being the most strongly adsorbed by the microgel particles at pH 8). The adsorption equilibrium was re-established for the microgel plus C10-OS system at pH 8, in a series of identical sample tubes. The particles were then centrifuged in each tube and as much of the supernatant was removed as possible. This was replaced with water in each tube. The systems were recentrifuged at increasing intervals from this time, and the new equilibrium concentration of C10-OS in each tube was determined. In this way the desorption kinetics, as well as the maximum extent of desorption, could be established. The results are shown in Figure 12. It is clear that for C10-OS the maximum desorbed amount is about 80% on dilution of the system into a large excess of water. This is again indicative of the strong hydrophobic association of the C10-OS molecules within the microgel particles. The comparatively long desorption time required (~10 min) would also support this suggestion. Finally, it is of interest to note that, as C10-OS is a colored molecule, the microgel particles themselves become colored when the organic salts are absorbed into them. This color is largely retained by the microgel particles even after 80% of the organic salt has been removed from the particles by dilution with a large excess of water and the system has been centrifuged to observe the microgel sediment.

CONCLUSIONS

Insertion of a C_x (x = 4, 6, 8, or 10) hydrocarbon chain between the diphenylazo moiety and the quaternary ammonium headgroup of the organic salts used in this work modifies the hydrophobic nature of the salt. This effect increases strongly from x = 4 to 10. Only the x = 6 and 8 cations of the organic salt absorb sufficiently strongly to reverse the charge of the (anionic) PNIPAM-*co*-AAc microgel particles at pH 8. The x = 10 organic salt is the most hydrophobic of the series and would reverse the charge, if its solubility in water were not so limited. Desorption of the x = 4 and 6 organic salts occurs readily on changing, in situ, the pH from 8 to 2.5 (and thereby eliminating the electrostatic attraction) but is only partially achieved for the x = 8 and 10 organic salts. Indeed for the x = 10 organic salt, only about 80% of the organic salt is desorbed upon dilution of the microgel particles into a large excess of water. Being able to introduce a controlled degree of hydrophobicity into otherwise essentially hydrophilic organic salts in the way described in this paper, and hence modify their uptake and release properties into microgel particles, has clear implications for controlled release applications of such microgel particles.

ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR and mass spectra for the organic salts. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author
*E-mail: melanie.bradley@bristol.ac.uk.

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