Water-Soluble Porous Nanospheres

Fred Henselwood and Guojun Liu*

Department of Chemistry, The University of Calgary, 2500 University Drive, NW, Calgary, Alberta, Canada T2N 1N4

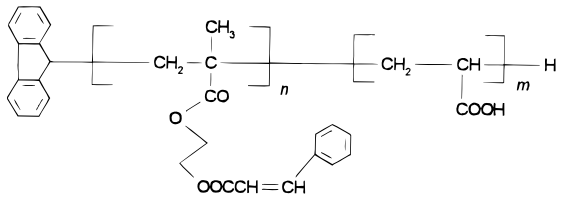
Received February 13, 1998; Revised Manuscript Received April 27, 1998

ABSTRACT: Poly[(2-cinnamoylethyl methacrylate)-*random*-(2-octanoylethyl methacrylate)]-*block*-poly(acrylic acid) [P(CEMA-*r*-OEMA)-*b*-PAA] forms micelles in water with P(CEMA-*r*-OEMA) as the core and PAA as the shell. POEMA is incorporated into the micellar cores. After PCEMA cross-linking, POEMA is extracted to produce porous water-soluble P(CEMA-*r*-OEMA)-*b*-PAA nanospheres. The porous nanospheres sorb a significantly higher amount of perylene from water/acetone and water/acetone/DMSO mixtures than the nonporous P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

I. Introduction

Due to their potential use in controlled drug release, water-soluble block copolymer micelles have attracted much attention recently.[1−8] In controlled drug release, a drug is first loaded into the core of the micelles and then released in a controlled fashion at the target site.[9]

We recently prepared micelles from poly(2-cinnamoylethyl methacrylate)-*block*-poly(acrylic acid) (PCEMA-*b*-PAA), in warm water, with PCEMA as the core and PAA as the corona.[10−12] The photo-cross-linking of the

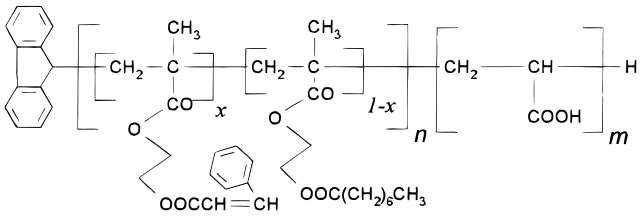


PCEMA-*b*-PAA

PCEMA cores allowed the preparation of "permanent micelles" or "nanospheres". A potential advantage of the nanospheres over micelles is their stability in all organic solvents. This allows the loading of a drug into the nanospheres by equilibrating the nanospheres with a concentrated drug solution in an organic solvent, in which a diblock micelle may disintegrate. In this paper, we illustrate another advantage for core cross-linking by showing the preparation of "porous nanospheres". These porous nanospheres should be particularly advantageous in controlled drug release, because the pores should allow the loading of more drugs.

Porous spheres with nano- to micrometer diameters are generally prepared from emulsion or microemulsion polymerization.[13−16] In one method, a porogen consisting of an organic solvent or a hydrophobic linear polymer is added to the emulsion polymerization mixture.[13−15] The organic solvent porogen should be so chosen that it phase segregates from the polymer formed during the emulsion polymerization. The pores are obtained after the evaporation of the organic solvent porogen from the cross-linked spheres. In the case of polymeric porogens, the porogens are removed by solvent extraction from the cross-linked spheres to yield pores. In another method, carboxyl groups are introduced via, for example, the copolymerization of acrylic acid into the microspheres generated from emulsion polymerization. Upon neutralization with a base, the poly(acrylic acid) regions swell due to electrostatic repulsion between different carboxyl groups to yield pores.[16] More recent achievements include the preparation of "nanosponges" from cross-linking high molar mass polymer chains intramolecularly[17] and vesicle formation from block copolymers in block-selective solvents.[18−22]

In this study, porous nanospheres were prepared from poly[(2-cinnamoylethyl methacrylate)-*random*-(2-octanoylethyl methacrylate)]-*block*-poly(acrylic acid) [P(CEMA-*r*-OEMA)-*b*-PAA]: where the first block consists of



a random copolymer of CEMA and OEMA at molar fractions of x and $1 - x$, respectively. Micelles of the above diblock were prepared in water containing an OEMA oligomer as the porogen in the P(CEMA-*r*-OEMA) core. After UV cross-linking of PCEMA, the POEMA porogen was extracted, leaving pores in the nanosphere cores. Presented is evidence for pore formation. The data obtained for perylene (a model compound for drugs) loading into the porous nanospheres will be compared against that found for the nonporous nanospheres.

II. Experimental Section

Polymer Synthesis. The precursor to P(CEMA-*r*-OEMA)-*b*-PAA was a poly(2-hydroxylethyl methacrylate)-*block*-poly(*tert*-butyl acrylate) (PHEMA-*b*-P*t*BA) sample with 3.6×10^2 units of HEMA and 5.6×10^2 units of *t*BA. PHEMA-*b*-P*t*BA with the hydroxyl groups protected by trimethylsilyl was synthesized by anionic polymerization as described previously.[11,23] To prepare P(CEMA-*r*-OEMA)-*b*-PAA, PHEMA-*b*-P*t*BA, ∼5 wt % in pyridine, was reacted with freshly distilled octanoyl chloride (Aldrich, 99%) for 2 h at 21 °C. Subsequently added was 1.5 times excess of cinnamoyl chloride (Aldrich, 98%), and the mixture was left to react for an additional 16 h. The polymer was precipitated into water, dissolved in THF, and precipitated into a methanol/water mixture (v/v = 3/1).

S0024-9297(98)00232-0 CCC: $15.00
Published on Web 06/10/1998

Table 1. Characteristics of the Polymers Used

polymer	n/m from NMR	$\bar{M}_w$ from GPC (g/mol)	$\bar{M}_w/\bar{M}n$ from GPC	x	10^{-5} $\bar{M}_w$ from LS (g/mol)	10^{-2} n	10^{-2} m
PCEMA-*b*-P*t*BA	0.65	6.9×10^4	1.07		1.66	3.6	5.6
P(CEMA-*r*-OEMA)-*b*-P*t*BA				0.70			
POEMA[a]		8.2×10^3	1.12				

[a] The precursor polymer, PHEMA, was reacted with cinnamoyl chloride to produce PCEMA, and the PCEMA analysis results are shown here.

The *tert*-butyl group of the P*t*BA block was cleaved following a method described previously.[24,25]

POEMA was prepared by reacting excess octanoyl chloride with PHEMA in pyridine at room temperature. The precursor, PHEMA, to the OEMA oligomer sample was also prepared by anionic polymerization.

The samples used were characterized by NMR, GPC, and light-scattering techniques. GPC was run in THF on a HT4 (Waters) column using polystyrene as the standard. Light scattering was conducted using a Brookhaven model 9025 instrument equipped with a 150-mW argon-ion laser operated at 488 nm.

Nanosphere Preparation and Characterization. Nonporous P(CEMA-*r*-OEMA)-*b*-PAA nanospheres, Nanosphere 1, were prepared following the traditional method.[10−12] Micelles with PAA as the shell and P(CEMA-*r*-OEMA) as the core were prepared by heating the P(CEMA-*r*-OEMA)-*b*-PAA sample in water at 80 °C overnight. PCEMA in the core was then cross-linked by light which had passed through a 260-nm cutoff filter from a 500-W Hg lamp. The conversion of CEMA as estimated from UV absorption analysis was 30%.[26]

For porous nanosphere preparation, 100 mg of POEMA and 75 mg of P(CEMA-*r*-OEMA)-*b*-PAA were mixed in 5 mL of acetone. A total of 20 mL of water was then added dropwise before another 80 mL was added in one aliquot. After acetone was driven off at 60 °C, the aqueous mixture was sealed and stirred at 80 °C for 16 h to establish the micelle size redistribution equilibrium. Upon cooling, the solution was purged with argon and irradiated to lock in the micellar structure to yield Nanosphere 2. The CEMA conversion was 36%.

The aqueous solution was then stirred with 100 mL of dichloromethane for 24 h to extract POEMA from the nanosphere cores. This process was repeated three times. After concentrating by rotary evaporation, the aqueous portion was added into acetonitrile to precipitate out the nanospheres. The nanospheres, denoted as Nanosphere 3, were dried under vacuum. The CH_2Cl_2 portion was dried for mass and NMR analysis.

Transmission electron microscopy (TEM) and dynamic light scattering were used to characterize the nanospheres. TEM specimens were prepared by aspirating a fine spray of an aqueous nanosphere solution using a home-built device[22] onto a Formvar-coated copper grid. The samples were stained by OsO_4 and viewed with a Hitachi-7000 electron microscope operated at 100 kV. For dynamic light-scattering measurements, the nanospheres were dissolved in dimethyl sulfoxide (DMSO) or water and centrifuged at 4500 rpm for half an hour to remove dust.

Fluorescence Measurements. All fluorescence measurements were carried out on a Photon Technology International Alpha Scan system equipped with a 75-W xenon lamp. Emission spectra were obtained by exciting at 410 nm.

Perylene Uptake by the Nanospheres. The maximum amount of perylene uptaken by a unit mass of nanospheres was measured under three sets of conditions. In case one, an aqueous nanosphere solution, 4.00 mL at 80 mg/L, was mixed with 2.00 mL of a perylene solution in acetone at 130 mg/L. The resulting solution was heated at 40 °C for 24 h before acetone was removed by gentle evacuation. After heating at 40 °C for another 2 days, the aqueous solution was filtered through either a filter paper or a nylon filter with a pore size of 5 μm to remove suspended perylene particles. The perylene-loaded nanospheres were then precipitated with the addition of 0.10 mL of a 1.0 M $CaCl_2$ solution, where Ca^{2+} may complex with acrylic acid groups from different nanospheres. The precipitated nanospheres were collected by filtration and the perylene was extracted from the nanospheres with 10.00 mL of THF for fluorescence intensity measurement. For more accurate results, a control experiment was also performed. In this case, 4.00 mL of water (instead of a nanosphere solution) was mixed with 2.00 mL of a perylene solution in acetone. The mixture was subjected to the same treatment as the nanosphere/perylene mixture. After the addition of $CaCl_2$, the solution was filtered and the trace amount of perylene on the filter paper was extracted with THF for fluorescence intensity analysis. As expected, this control sample accounted for a small fraction, e.g., <5%, of the fluorescence intensity for the samples. The fluorescence intensity resulting from perylene trapped in the nanospheres was obtained by taking the difference between those of the sample and the control. The concentration of perylene in THF extracted from the nanospheres was determined by comparing its intensity with those of samples in THF with known perylene concentrations.

In case two, 0.20 mL of DMSO was added to the 4.00-mL nanosphere and 2.00-mL perylene solution mixture. The mixture was then subjected to the same treatment as that described in case one. Unlike acetone, DMSO should have survived the evacuation step.

In case three, a perylene solution in acetone, 2.10 mg/L, was added to a clean sample vial. The acetone was evaporated, and to the vial was added 4.00 mL of a nanosphere solution at ~0.07 mg/mL. The vial was subsequently capped, wrapped in aluminum foil, and stirred for 3 weeks to establish perylene partition equilibrium. Perylene fluorescence intensity was measured to evaluate the amount of perylene adsorbed, after the sample was centrifuged at 1500 rpm for 10 min to remove the excess perylene particles which were not solubilized and the perylene was extracted from the nanospheres.

III. Results and Discussion

Polymer Characteristics. Reacting the precursor diblock, PHEMA-*b*-P*t*BA, with cinnamoyl chloride yielded PCEMA-*b*-P*t*BA. The PCEMA-*b*-P*t*BA sample was characterized by GPC, NMR, and light scattering (LS), and their results are summarized in Table 1. Since polystyrene samples were used as the calibration standards, the GPC molar masses are approximate. Only the weight-average molar mass, $\bar{M}_w$, for PCEMA-*b*-P*t*BA was used to calculate the number of CEMA units, n, and *t*BA units, m. Since the P(CEMA-*r*-OEMA)-*b*-PAA sample was derived from the same PHEMA-*b*-P*t*BA sample, P(CEMA-*r*-OEMA)-*b*-PAA should be monodisperse as well with a total of 3.6×10^2 units of CEMA and OEMA and 5.6×10^2 units of AA, if the hydrolysis efficiency of *t*BA is assumed to be 100% (approximately quantitative as shown experimentally previously).[10,11] Illustrated in Figure 1 is a ^{1}H NMR spectrum of the P(CEMA-*r*-OEMA)-*b*-P*t*BA sample. From ratioing the peak intensities of OEMA to those of CEMA, we obtained a CEMA molar fraction, x, of 0.70. Thus, the numbers of CEMA and OEMA units in a polymer chain are 2.5×10^2 and 1.1×10^2, respectively.

The total number of OEMA units in a POEMA chain was estimated to be 33 from NMR by ratioing the ^{1}H peak intensities of OEMA to the terminal fluorenyl group (fluorenyllithium was used as the initiator for

[PCEMA-*r*-POEMA]-*b*-P*t*BA

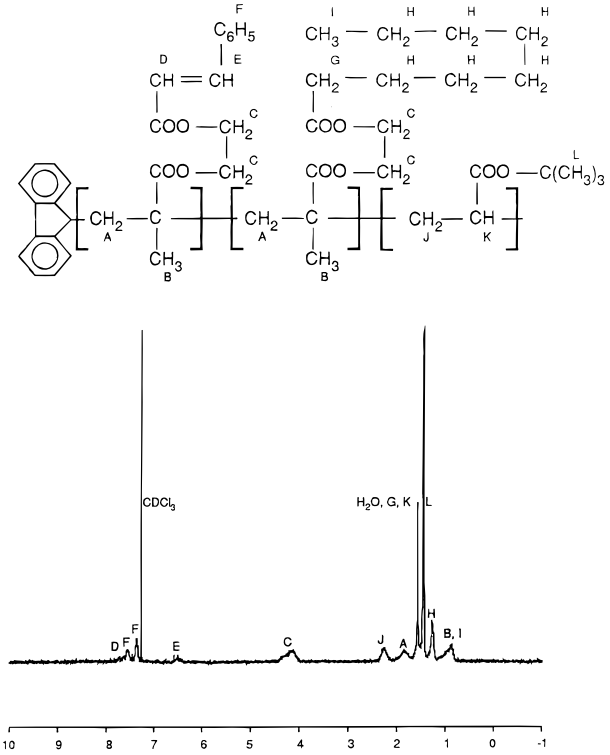


Figure 1. Proton NMR spectrum of a P(CEMA-*r*-OEMA)-*b*-P*t*BA sample with an OEMA molar fraction of 30% in $CDCl_3$.

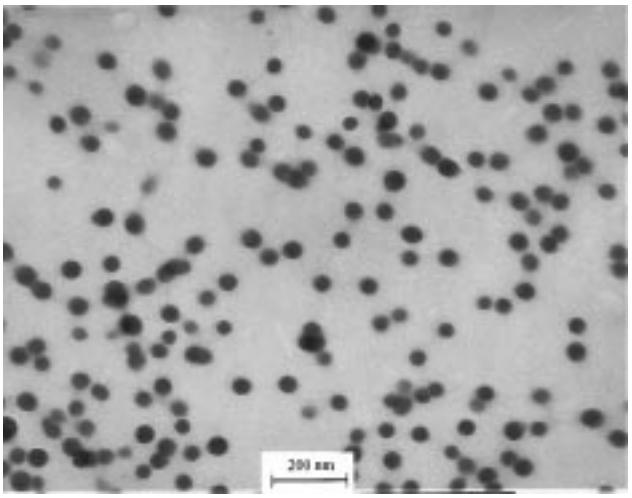


Figure 2. TEM image of nonporous P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

2-(trimethylsilyl)ethyl methacrylate polymerization). GPC analysis indicates that the sample has a narrow molar mass distribution (Table 1).

Nonporous P(CEMA-*r*-OEMA)-*b*-PAA Nanospheres. Nonporous nanospheres were prepared previously from this P(CEMA-*r*-OEMA)-*b*-PAA sample.[12] The spherical shape of the particles is evident from the TEM image shown in Figure 2, and the nanospheres have a narrow size distribution. Dynamic light-scattering measurements in DMSO gave a hydrodynamic radius of 65 ± 2 nm for the nanospheres (Table 2).

POEMA-Loaded P(CEMA-*r*-OEMA)-*b*-PAA Nanospheres. Illustrated in Figure 3 is a TEM image of the POEMA-loaded P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

Table 2. Characteristics of the Nanospheres

sample[a]	CEMA conv. (%)	TEM diameter (nm)	R_h (nm)[b] in 0.10 M HCl	R_h (nm) in DMSO
Nanosphere 1	30			65 ± 2
Nanosphere 2	36	39 ± 3	71.5 ± 0.4	
Nanosphere 3	36	39 ± 3	70.5 ± 0.4	62 ± 2

[a] Nanospheres 1, 2, and 3 are the P(CEMA-*r*-OEMA)-*b*-PAA, POEMA-loaded P(CEMA-*r*-OEMA)-*b*-PAA, and porous nanospheres, respectively. [b] R_h was determined at the scattering angle of 90°.

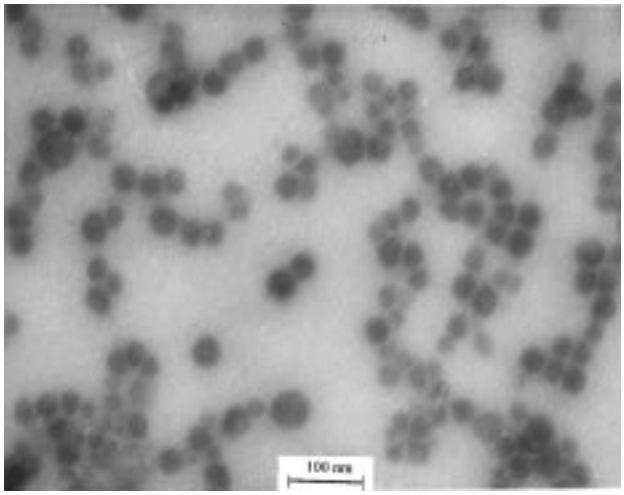


Figure 3. TEM image of POEMA-loaded P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

The diameter as averaged over 120 particles is 39 ± 3 nm.

The contrast between the particles and the background in Figure 3 is not as sharp as that in Figure 2. This suggests the incorporation of POEMA into the cores, because POEMA does not contain any aliphatic double bonds and is not as readily stained by OsO_4 as PCEMA. The incorporation of POEMA into the P(CEMA-*r*-OEMA) core of the micelles can be further appreciated from the following observation. POEMA is not soluble in water and did not phase segregate in the system after the micelles were prepared. When a similar experiment was performed to incorporate polyisoprene (PI) into the cores, the PI polymer precipitated out. The POEMA was stabilized by the core probably because of OEMA units in the core block.

Preparation of Porous P(CEMA-*r*-OEMA)-*b*-PAA Nanospheres. Illustrated in Figure 4 is a TEM image of the porous nanospheres. The particles are spherical. The presence of pores is, however, difficult to discern from the TEM picture. An indirect but definitive piece of evidence for pore formation derives from the fact that POEMA was extracted from the nanospheres but the CH_2Cl_2 extraction step did not decrease the nanosphere size.

As mentioned in the Experimental Section, extraction of the POEMA-loaded nanospheres with CH_2Cl_2 removed 85% of the initially added POEMA from the nanospheres. Since 100 mg of POEMA was mixed with 75 mg of the P(CEMA-*r*-OEMA)-*b*-PAA sample and the weight fraction of P(CEMA-*r*-OEMA) in P(CEMA-*r*-OEMA)-*b*-PAA is 70%, the removal of 85 mg of POEMA from such cores with a total mass of 152.5 mg should shrink the core size by a factor of $(85/152.5)^{1/3}$ or 0.82, if the density of the cores remains constant before and after POEMA extraction or if the cores after POEMA

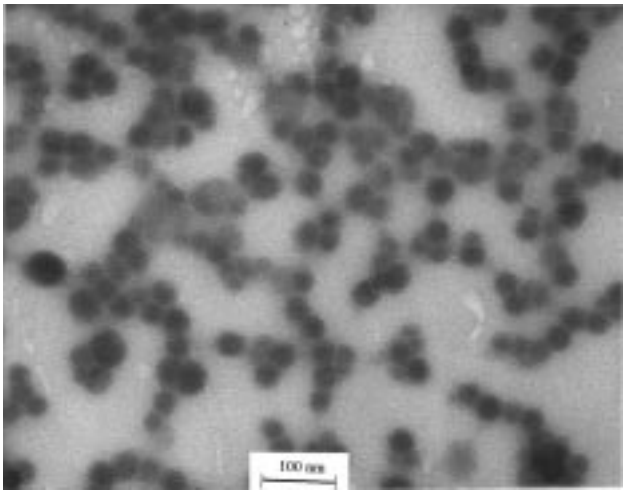


Figure 4. TEM image of porous P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

removal are not porous. In reality, the core diameter as averaged over 120 particles from Figure 4 is 39 ± 3 nm, the same as the core size before POEMA extraction. Thus, the space once occupied by POEMA must have been left behind as voids in the nanospheres.

The hydrodynamic radii of the porous and POEMA-loaded P(CEMA-*r*-OEMA)-*b*-PAA nanospheres were determined by dynamic light scattering in a 0.10 M HCl solution to be 71.5 ± 0.4 and 70.5 ± 0.5 nm. Again, there is little variation in the particle sizes (Table 2) with the removal of POEMA from the nanospheres.

The hydrodynamic radius is substantially larger than the TEM radius, because the PAA layer should swell in the HCl solution. Furthermore, the radius determined from TEM may only represent that of the core, because PAA is not stained by OsO_4.

Perylene Uptake Capacities. Perylene is a molecule with five fused benzene rings and is similar in size to that of many drug molecules. We tested if more perylene could be loaded into the porous nanospheres than into the nonporous P(CEMA-*r*-OEMA)-*b*-PAA nanospheres.

To load the nanospheres with perylene, perylene and the nanospheres were stirred in water/acetone (v/v = 2/1) or water/acetone/DMSO (v/v/v = 20/10/1) mixtures. Acetone was subsequently removed. After stirring the resultant aqueous mixture for another 2 days to ripen the perylene crystals, solid perylene was filtered off and the nanospheres were precipitated. The amount of perylene trapped in the nanospheres was determined by analyzing the fluorescence intensity of perylene in THF or benzene after the extraction of perylene from the nanospheres. Shown in Table 3 are the perylene loading capacities, in units of g/g, of both the porous and nonporous nanospheres determined under these conditions from several trials. The difference between the capacity of the porous and nonporous nanospheres is substantial and consistent. Thus, the porous nanospheres showed an increased capacity for perylene uptake under these conditions. This increase has to be explained by the presence of pores in the porous nanospheres, because the two types of nanospheres are otherwise the same structurally.

An explanation of the observed capacity differences would require more information about the pore shape, size, and size distribution in acetone/water, which should be determined in a future study. We here

Table 3. Comparison of the Perylene Uptake Capacities of Nanospheres 1 and 3[a]

trial	capacity of Nanosphere 1 (g/g)	capacity of Nanosphere 3 (g/g)	difference
	Loading Medium: $V_{Acetone}/V_{Water} = 1/2$		
1	17%	36%	53%
2	16%	27%	41%
3	23%	30%	23%
4	10%	19%	47%
average	(16.5 ± 5.4)%	(28 ± 7)%	(41 ± 13)%
	Loading Medium: $V_{Acetone}/V_{Water}/V_{DMSO} = 10/20/1$		
1	40%	49%	18%
	Loading Medium: Water		
1	0.4%	0.4%	0%

[a] The capacities are taken as the mass of perylene uptaken by each gram of nanosphere core.

explain the capacity difference based on the assumption that the pores are sufficiently large and are present even in acetone/water, in which the cross-linked P(CEMA-*r*-OEMA) swells to a degree. In the pores, the acetone content may be higher than that in the bulk due to effect of their hydrophobic walls. It is the solubilization of perylene in the solvent mixtures held in the pores which helps increase the perylene uptake capacity. This also explains why no increase in perylene uptake capacity was observed experimentally for the porous nanospheres when the perylene loading experiment was performed in water (Table 3).

Higher Perylene Uptake Capacities in Acetone/Water. The capacity of perylene uptake in water/acetone (1/2) by the nonporous PCEMA-*b*-PAA nanosphere cores is ~0.16 g/g. This represents a 40-fold increase over that determined in water for the nanosphere. The perylene partition equilibrium can be expressed by

$$\mathrm{P(s)} \rightleftharpoons \mathrm{P(w)} \overset{K}{\rightleftharpoons} \mathrm{P(N)} \tag{1}$$

where P(s), P(w), and P(N) represent solid perylene and perylene in the solution phase and in the nanosphere cores, respectively. The perylene partition coefficient K is

$$K = \frac{\gamma_{\mathrm{P(N)}}[\mathrm{P(N)}]}{\gamma_{\mathrm{P(w)}}[\mathrm{P(w)}]} \tag{2}$$

with γ denoting the activity coefficient of each component. If an excess of solid perylene is used, the perylene concentration in the solution phase should be equal to its solubility. The perylene uptake capacity increases in acetone/water for the nonporous nanospheres probably due to a drastic increase in [P(w)]. Also, the PCEMA cores should swell more in acetone/water than in water, which increases the volume fraction for the hydrophobic phase and partially accounts for the observed perylene uptake capacity increase.

Scatter in Perylene Uptake Capacity Data. The perylene uptake capacities as seen in Table 3 vary significantly from trial to trial for a given sample. Our later studies revealed that this might have been caused by the different times used to ripen the perylene crystals after acetone evaporation.

As is discussed in the previous subsection, the perylene uptake capacity increased in acetone/water over that in water probably because of increased solubility of perylene in the acetone/water mixture. Perylene loading was

achieved by us in an acetone/water mixture. However, acetone was evaporated to reduce perylene solubility in the solution phase before the free perylene was filtered out. After acetone evaporation, [P(w)] should decrease, which decreases [P(N)] if K does not decrease as much as [P(w)]. It was found experimentally that the perylene uptake capacity did decrease with the time lag between acetone evaporation and perylene filtration. While this time lag changed from trial to trial, it was, however, approximately the same for each pair of porous and nonporous nanosphere samples. Thus, the capacity difference between a given pair is real.

IV. Conclusions

POEMA was incorporated into the core of aqueous P(CEMA-*r*-OEMA)-*b*-PAA micelles. After the photo-cross-linking of the cores, POEMA could be extracted by CH_2Cl_2. Since the size of the micellar cores and the hydrodynamic radius of the micelles did not change with POEMA removal, as confirmed by our TEM and dynamic light-scattering results, the space originally occupied by POEMA must have been left behind as pores in the nanosphere cores. The presence of the pores was further confirmed by the higher perylene uptake capacity of the porous nanospheres than the nonporous nanospheres in water/acetone or water/acetone/DMSO mixtures. A future study should involve the pore size, size distribution, pore volume, and inner surface area determination for direct proof of pore formation in the nanosphere cores.

Acknowledgment. The Natural Sciences and Engineering Research Council of Canada is acknowledged for financially sponsoring this research.

References and Notes

(1) (a) Tuzar, Z. *Solvents and Self-Organization of Polymers*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1996. (b) Nagarajan, R. *Solvents and Self-Organization of Polymers*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1996.
(2) Shen, H.; Zhang, L.; Eisenberg, A. *J. Phys. Chem. B* **1997**, *101*, 4697.
(3) Chen, W.-Y.; Alexandridis, P.; Su, C.-K.; Patrickios, C. S.; Hertler, W. R.; Hatton, T. A. *Macromolecules* **1995**, *28*, 8604.
(4) Alexandridis, P.; Olsson, U.; Lindman, B. *Macromolecules* **1995**, *28*, 7700.
(5) Chu, B. *Langmuir* **1995**, *11*, 414.
(6) Qin, A.; Tian, M.; Ramireddy, C.; Webber, S. E.; Munk, P.; Tuzar, Z. *Macromolecules* **1994**, *27*, 120.
(7) Ikemi, M.; Odagiri, N.; Tanaka, S.; Shinohara, I.; Chiba, A. *Macromolecules* **1981**, *14*, 34.
(8) Xu, R.; Winnik, M. A.; Riess, G.; Chu, B.; Croucher, M.-D. *Macromolecules* **1992**, *25*, 644.
(9) Cammas, S.; Kataoka, K. *Solvents and Self-Organization of Polymers*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1996.
(10) Henselwood, F.; Liu, G. *Macromolecules* **1997**, *30*, 488.
(11) Wang, G.; Henselwood, F.; Liu, G. *Langmuir* **1998**, *14*, 1554.
(12) Henselwood, F.; Liu, G. *J. Appl. Polym. Sci.* **1998**, in press.
(13) See, for example: Horak, D.; Benes, M. J. *Polymer Materials Encyclopedia*; CRC Press: Boca Raton, FL, 1996; p 3949.
(14) See, for example: Wang, Q. C.; Svec, F.; Fréchet, J. M. J. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 2577.
(15) See, for example: He, B.; Zhang, Z.; Quian, T. *Gaofenzi Tongxun* **1982**, *4*, 278.
(16) Okubo, M. *Polymer Materials Encyclopedia*; CRC Press: Boca Raton, FL, 1996; p 4537.
(17) Davankov, V. A.; Ilyin, M. M.; Tsyurupa, M. P.; Timofeeva, G. I.; Dubrovina, L. V. *Macromolecules* **1996**, *29*, 8398.
(18) Zhang, L.; Eisenberg, A. *Science* **1995**, *268*, 1728.
(19) Ding, J.; Liu, G. *J. Phys. Chem.* **1998**, in press.
(20) Ding, J.; Liu, G. *Chem. Mater.* **1998**, *10*, 537.
(21) Ding, J.; Liu, G. *Polymer* **1997**, *38*, 5497.
(22) Ding, J.; Liu, G. *Macromolecules* **1997**, *30*, 655.
(23) Liu, G.; Smith, C. K.; Hu, N.; Tao, J. *Macromolecules* **1996**, *29*, 220.
(24) Liu, G.; Ding, J.; Guo, A. *Macromolecules* **1997**, *30*, 1851.
(25) Smith, C.; Liu, G. *Macromolecules* **1996**, *29*, 2060.
(26) Guo, A.; Tao, J.; Liu, G. *Macromolecules* **1996**, *29*, 2487.

MA9802327