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Hairy, Semi-shaved, and Fully Shaved Hollow Nanospheres from Polyisoprene-*block*-poly(2-cinnamoylethyl methacrylate)

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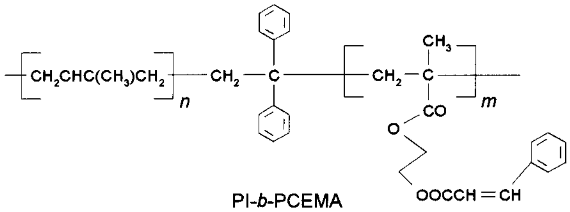
A polyisoprene-*block*-poly(2-cinnamoylethyl methacrylate) (PI-*b*-PCEMA) sample formed vesicles in THF/hexanes with a THF volume fraction of 20%. In such vesicles, PCEMA made up the essentially-solvent-free spherical shell and the PI chains stretched into the solution phase from both the inner and outer PCEMA surfaces. Hairy hollow nanospheres were prepared by photo-cross-linking the PCEMA shell. Treating the cross-linked vesicles with ozone for a short period selectively degraded the outer PI chains to yield semi-shaved hollow nanospheres. Fully shaved hollow nanospheres were prepared by degrading both the inner and outer PI chains using long ozonolysis times. Due to the poor solubility of the fully shaved hollow nanospheres in common organic solvents, they may be useful as macroporous resins in chemical separations.

I. Introduction

In a block-selective solvent, which is good for one but poor for the other block, a diblock copolymer may form vesicles with the soluble block in contact with the solvent to stabilize the collapsed insoluble block. The vesicles formed can be spherical,[1,2] cylindrical,[3−5] vesicular,[5−7] or toroidal.[7] Like conventional diblock copolymers, polyisoprene-*block*-poly(2-cinnamoylethyl methacrylate) (PI-*b*-PCEMA) forms various micelles in solvents selectively good for the PI block.[6,7] In a vesicle, PCEMA makes up the essentially-solvent-free spherical shell, and the PI chains stretch into the solvent phase both from the inner and outer PCEMA surfaces. In this paper, we report the preparation of “permanent” vesicles or “hairy” hollow nanospheres by photo-cross-linking the PCEMA skeleton. “Semi-shaved” or “fully shaved” hollow nanospheres were prepared by cleaving off the PI chains on the outer surface only or on both the outer and inner surfaces. This work was initiated mainly to demonstrate the synthetic control one has in nanoengineering. Also, the fully shaved and half-shaved nanospheres may be useful as macroporous resins for chemical separations.[8]


PI-*b*-PCEMA

II. Experimental Section

Polymer Synthesis and Characterization. PI-*b*-PCEMA was prepared by reacting PI-*b*-PHEMA, where PHEMA denotes poly(2-hydroxylethyl methacrylate), with excess cinnamoyl chloride in pyridine at room temperature. The precursor to PI-*b*-PHEMA was PI-*b*-P(HEMA−TMS) where P(HEMA−TMS) denotes poly(trimethylsiloxylethyl methacrylate). PI-*b*-P(HEMA−TMS) was prepared by anionic polymerization.[6,9] PI-*b*-PCEMA was characterized by NMR, GPC, and light scattering as described previously,[9] and the results are shown in Table 1.

Instrumentation and Techniques. Gel permeation chromatographic analysis was performed using THF as the eluant. The Styragel HT-4 (Waters) column used was calibrated using polystyrene standards. Light scattering was done using a Brookhaven Model 9025 instrument equipped with an argon-ion laser operated at 488 nm.

Vesicle Preparation. PI-*b*-PCEMA was dissolved molecularly in THF/hexanes (HX) with 35% HX by volume. The solution was then slowly added into an equal volume of THF/HX with 85% HX to induce vesicle formation. The vesicle solution in THF/HX with 60% HX was equilibrated for 1−2 weeks before an equal volume of HX was added to yield a vesicle solution at the concentration of ~1.0 mg/mL in THF/HX with 80% HX. The solution was immediately irradiated to “lock in” the vesicles. The vesicles were initially prepared in THF/HX with 60% HX because the vesicles in this mixture had the lowest polydispersity as shown by TEM and dynamic light-scattering results. More HX was added just before irradiation so as to reduce the THF content in the solvent. Our previous studies have demonstrated that the chain-exchange rate increased with an increase in the content of the mutual solvent, THF, for the two blocks.[10] A fast chain exchange rate suggests the fluidity of the PCEMA shell. The

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Table 1. Characteristics of the PI-*b*-PCEMA Sample

n/m from NMR	$\bar{M}_w/\bar{M}_n$ from GPC	$10^{-4}\bar{M}_w$ (g/mol) GPC	dn_r/dc^a (mL/g)	$10^{-4}\bar{M}_w{}^a$ (g/mol) LS	$10^{-2}n$	$10^{-2}m$
0.38	1.19	2.7	0.150	6.6	0.88	2.3

[a] Light-scattering experiment was performed in chloroform.

vesicle structure should be made sufficiently rigid so that they do not fuse during photolysis.[11]

Photo-Cross-Linking and Ozonolysis. Photolysis was achieved with light from a 500-W mercury lamp which had passed through a 310-nm cutoff filter. The conversion of CEMA with irradiation was followed by UV absorbance analysis at 274 nm.[2] The vesicles we used had a CEMA conversion of 40%. The cross-linked vesicles or "hairy hollow nanospheres" were concentrated and then purified by precipitation into methanol.

Cross-linked vesicles were dissolved in methylene chloride containing 5% methanol and then cooled to −40 °C. Ozone was bubbled through the vesicle solution for either 0.5 or 10 min, depending on whether semi-shaved or fully shaved hollow nanospheres were to be prepared, before the ozone was blown out of the solution by nitrogen. Excess trimethyl phosphite and a trace amount of 2,6-di-*tert*-butyl-4-methylphenol were then added, and the mixture was stirred for 2 days at −40 °C. Trimethyl phosphite was added to reduce the ozonides formed to ketone or carbonyl groups. 2,6-di-*tert*-butyl-4-methylphenol functioned as a free radical scavenger. The semi-shaved and fully shaved nanospheres were purified by precipitation into hexanes and the precipitate was then washed with methanol.

Viscosity and Refractive Index of THF/HX with 20% THF. The viscosity of the solvent mixture was measured to be 0.324 cP following a method described previously.[12] The refractive index increment of the solvent mixture relative HX was 0.006 as measured using a differential refractometer (Precision Instruments Co.). Using the refractive index of 1.372 at the sodium D line to approximate that of HX at 488 nm, we obtain a refractive index of 1.378 for the solvent mixture.

Light-Scattering Measurements. For R_h measurement, freshly precipitated semi- and fully shaved nanospheres were dissolved in THF and centrifuged for 10 min at 10 × 10^3 rpm using a centrifuge with a G value of 16 × 10^3. For static light-scattering studies of the hairy nanospheres, the sample was centrifuged at the spinning rate of 1.5 × 10^3 rpm.

Specific Refractive Index Increment, dn_r/dc. Measurement of the refractive index increment, Δn_r, of a vesicle solution in THF/HX with 80% HX, relative to the solvent at constant chemical potential, required the dialysis of the solution against the solvent. This was done by introducing 5.00 mL of a vesicle solution into a dialysis tube (Spectra/Por 4). The tube was equilibrated with the solvent (150 mL) for 48 h. Changes in polymer concentration due to dialysis were monitored by UV spectrophotometry at 274 nm.

The Δn_r values at 488 nm at room temperature were determined using the differential refractometer described above. The specific refractive index increment ν or dn_r/dc, where n_r and c represent the refractive index and concentration of a polymer solution, was obtained from the slope of plotting Δn_r vs c to be 0.180 mL/g.

TEM Measurements. Several drops of a vesicle or hollow nanosphere solution were added into a tube containing a capillary open end and a male ground joint close to the other end. The tube was inserted into a socket with the capillary end located at the narrowed exit end of the socket. As the solution dripped out of the capillary, air, introduced from the sidearm of the socket and gushing out of the exit, broke the fine droplet and brought the particles into contact with a Formvar-covered copper grid. Sprayed vesicles or nanospheres were stained with OsO_4 overnight and viewed by a Hitachi-7000 transmission electron microscope (TEM) operated at 10^5 V.

III. Results and Discussion

Vesicle Formation. Illustrated in Figure 1 is a TEM photograph of the PI-*b*-PCEMA vesicles prepared in hexanes/THF with 20% of THF. The circular image consists of a dark ring separating a light core from a shell of intermediate darkness.

To differentiate the reactivity of PCEMA and PI toward OsO_4, a film containing 10% of PI and 90% of PCEMA homopolymers was prepared. The film was then sliced, the slices were stained with OsO_4 and viewed by TEM. Since the domains of the minor component were darker, PI reacted with OsO_4 more readily.

To know the 3-D structure of the vesicles, we also obtained a TEM image of the vesicles shown in Figure 1 at the TEM sample stage tilting angle, α_t, of ~50° as shown in Figure 2. The tilting of the sample stage decreased the distances along the tilting direction, marked by a long arrow in Figure 2, between the projected images of different vesicles. For the two vesicles marked by two short arrows, the distance decreased by a factor of 0.67 which is approximately equal to cos α_t. The diameter of the central gray circle of each vesicle, however, did not vary with the tilting angle change. This suggests that the central part of the vesicles was spherical.

The overall vesicle would be spherical if not for the smeared periphery along the direction approximately normal to the tilting direction. This edge smearing suggests the deformation or flattening of the spherical vesicles at the point of contact with the Formvar support. The local deformation of a vesicle is understandable as a vesicle contained some solvent when first sprayed on to the Formvar support. A solvent-plasticized vesicle is deformable.

The vesicles are spherical but are not spheres with PCEMA as the core and PI as the shell, because this assignment cannot explain the presence of a dark ring between the shell and the core. Then, the weight fraction of 9.4% for PI is too low to explain the observed thickness of the shell. Similar structures were observed by TEM from polystyrene-*block*-poly(acrylic acid) dissolved in water, and the structures were shown by Zhang and Eisenberg to be vesicles.[5] Thus, the lighter centers of the particles in Figure 1 correspond to the cavities. The dark ring represents the location of a collapsed PI layer. The cavities should have been originally filled with the THF/hexanes mixture which swelled the PI chains.

Although not seen in Figure 1, a PI layer must have existed on the outer surface of the PCEMA shell for the vesicles to be stable in THF/hexanes. The outer PI layer is not discernible here probably because the PI layer on the outer surface is thin. The outer PI layer could be thin, because the outer layer occupies a much larger surface area. Drawing a very thin layer around a large sphere and lines through this thin layer, one will find that the path lengths of the lines through the thin layer are indeed short. Such short path lengths will not enable the efficient blockage of the TEM beams for the

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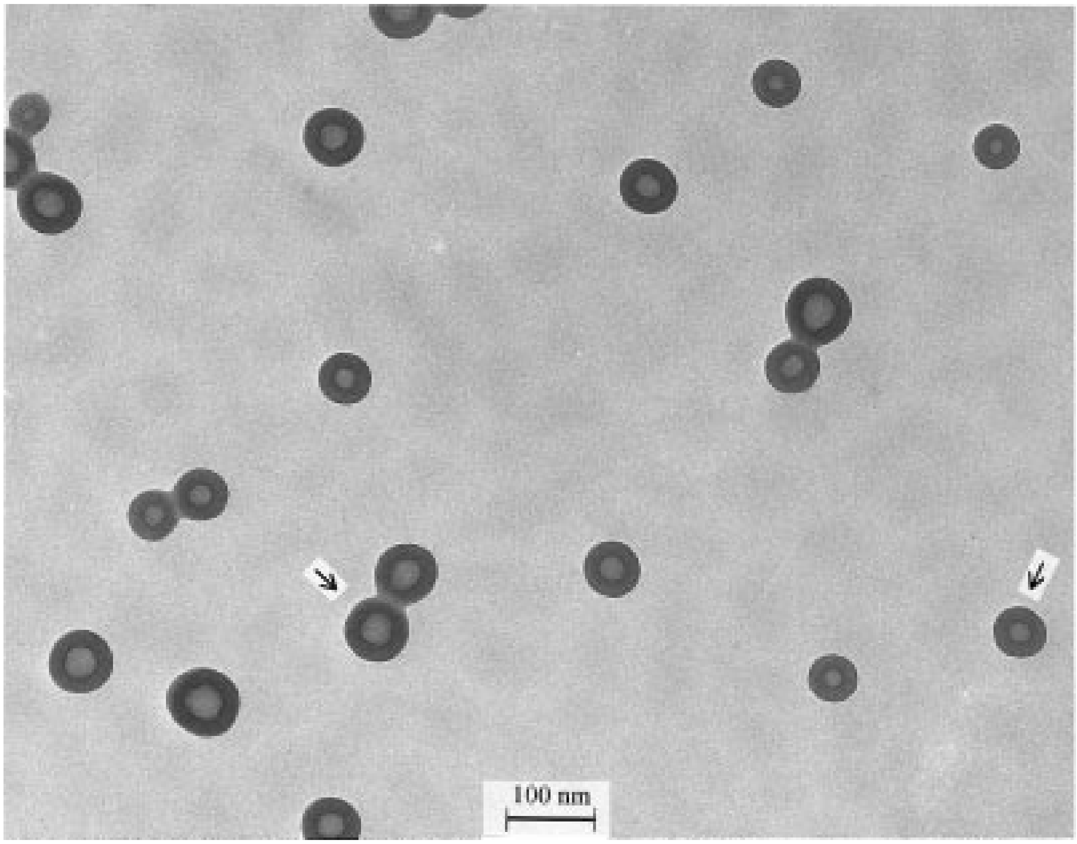

Figure 1. TEM image of PI-*b*-PCEMA vesicles prepared in hexanes/THF with 20% THF.

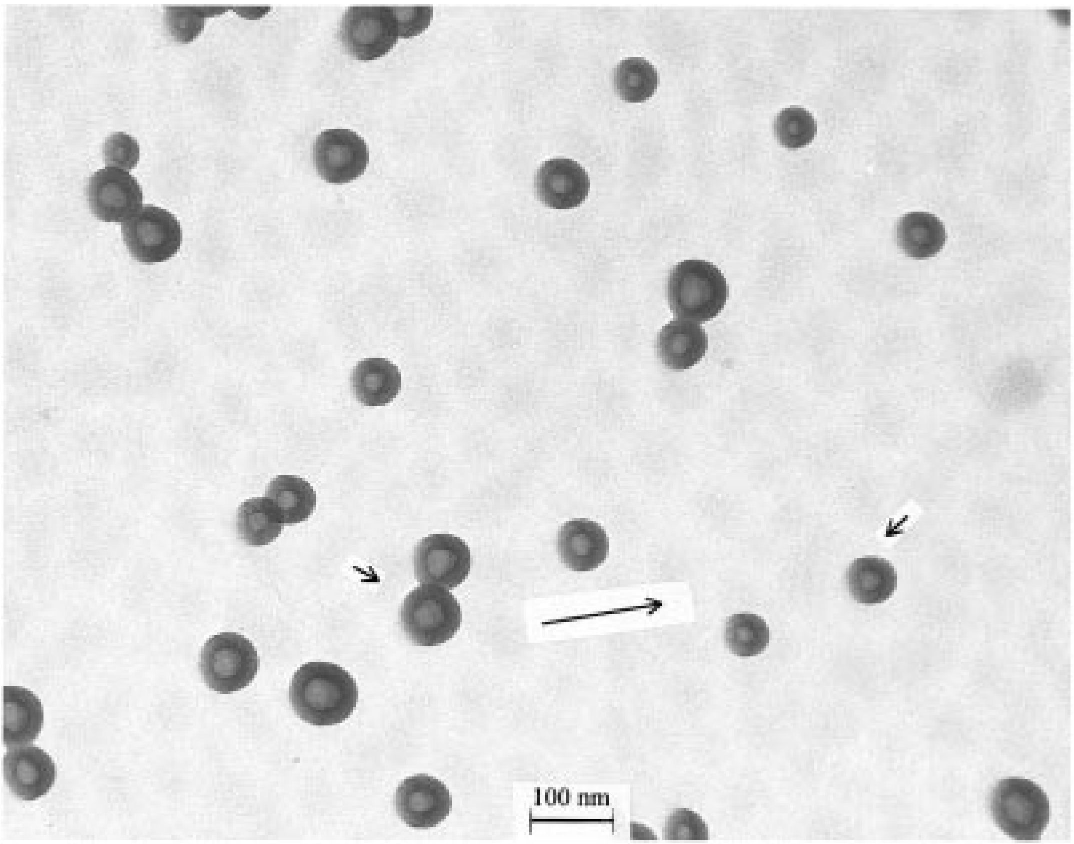

Figure 2. TEM images of the sample shown in Figure 1 viewed at the TEM sample stage angle ~50° tilted along the long arrow direction.

formation of a dark ring in the TEM image. The presence of a PI layer will become evident as we later report the selective shaving of the PI hairs on the outer surface by ozonolysis.

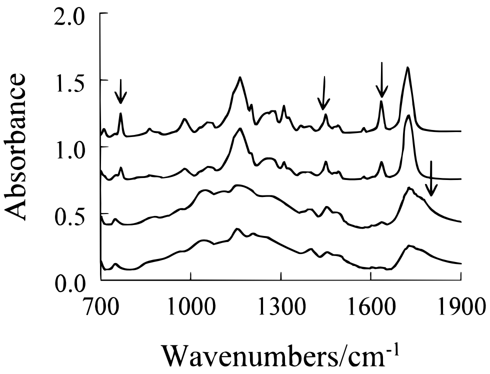

Figure 3. Comparison between FTIR spectra of PI-*b*-PCEMA (top), the PI-*b*-PCEMA vesicles at the CEMA conversion of 40% before ozonolysis (second from the top), treated with ozone for 0.5 min (third from the top), and 10 min (bottom).

Figure 1 clearly shows that the vesicles have a wider size distribution than some of the spherical vesicles we prepared previously.[13] They have a cavity and outer diameter of ~28 and ~70 nm, respectively. These cavities should be able to hold much drug, if the vesicles were to be used in controlled drug release.

Origin of the Vesicles. The TEM sample shown in Figure 1 was prepared by aspirating a fine spray PI-*b*-PCEMA in THF/hexanes on Formvar-covered grids. Due to the fast solvent evaporation rate, significant morphological change in the particles during solvent evaporation should not have been possible. PI-*b*-PCEMA vesicles in THF/hexanes mixtures with 20% THF were also irradiated with UV light to cause a CEMA conversion of 40%. Similar TEM images were obtained from these samples. Since cross-linked vesicles are very unlikely to undergo a fast morphological transition with solvent composition change during solvent evaporation, the vesicles of Figure 1 must have been present in the original hexanes/THF mixture.

Vesicle Cross-Linking. CEMA dimerizes due to photoinduced cycloaddition. PCEMA cross-links because of the dimerization among many CEMA groups of different chains.[14,15] The disappearance of the CEMA groups was followed by UV spectrophotometry, as CEMA absorbs strongly at 274 nm. The cross-linking of PCEMA could also be appreciated from the FTIR results shown in Figure 3. UV irradiation reduced the carbon−carbon double-bond peak intensity at 1635 and 770 cm^{-1} substantially.

The hydrodynamic radii, R_h, of the vesicles before and after UV irradiation were determined and are compared in Table 2. The fact that R_h decreased insignificantly, i.e., from 56 to 54 nm, suggests that the micellar morphology did not change with UV irradiation. It is very likely that the UV irradiation only “locked in” the structure of the vesicle and did not change the vesicle aggregation number either as in the cross-linking of spherical PS-*b*-PCEMA vesicles.[16]

Properties of the Hairy Hollow Nanospheres. Dried cross-linked vesicles were soluble in a wide range of solvents including THF, chloroform, toluene, etc. TEM results confirmed that the cross-linked vesicles retained their integrity in such solvents. The cross-linked vesicles, however, did aggregate with time in the solid state probably due to intervesicle linking through PI chains. This aggregation was confirmed by an increase in the molar mass and size of the cross-linked vesicles with storage time.

Light-scattering studies of the cross-linked vesicles were thus carried out in THF/HX with 20% THF immediately after they were prepared. The weight-average molar mass, $\bar{M}_w$, and radius of gyration, R_G, of the vesicles determined this way were 2.1 × 10^8 g/mol and 39 nm, respectively. Assuming a cavity radius, R_c, of 14 nm and a polymer density of $\rho = 1.0$ g/cm^3, this molar mass should give a vesicle outer radius, R_o, of 43 nm as calculated from

$$^4/_3\pi N_A\rho(R_o^{\,3} - R_c^{\,3}) = 2.1 \times 10^8 \text{ g/cm}^3 \qquad (1)$$

This R_o value compares well with 35 nm obtained from Figure 1, considering the relatively wide vesicle size distribution.

The hydrodynamic radius, R_h, of the hairy hollow nanospheres in THF/HX with 20% THF was measured over the scattering angle range 30−150° and the average value from these angles was 54 ± 1 nm. This gives $R_h/R_G = 1.38$, which is close to the theoretical value of 1.29 for homogeneous spheres.

Semi-shaved Hollow Nanospheres. Illustrated in Figure 4 is a TEM image of a nanosphere sample treated with ozone for 0.5 min. The cleaving of the outer PI block is clear here, because the outer boundary of the vesicles is now diffuse. The integrity of the inner PI block is demonstrated by the remaining dark ring separating the PCEMA skeleton and the cavity.

Also compared in Figure 3 are the FTIR spectra of the hairy and the semi-shaved hollow nanospheres. PI has a peak at 1451 cm^{-1} originating from the bending motion of the methyl groups in isoprene units. During CEMA cross-linking, the intensity of this peak remained unchanged as expected. The ozonolysis treatment caused a partial decrease in the intensity of this peak. The formation of carbonyl groups after ozonolysis is demonstrated by the appearance of a shoulder at 1781 cm^{-1} next to the ester carbonyl groups of PCEMA at 1715 cm^{-1}.

A decrease in the intensities of the peaks at 1635 and 770 cm^{-1} is also noticed. This suggests that the carbon−carbon double bonds of PCEMA were degraded by the ozonolysis treatment as well. To ensure the integrity of the PCEMA double bonds, one should use an even shorter ozone treatment time.

The shaving of the PI chains on the outer surface is also demonstrated by a decrease in R_h from 58 to 47 nm. Since each PI chain has ~88 isoprene units, this decrease in R_h or a PI thickness of 11 nm is reasonable.

The freshly precipitated semi-shaved hollow nanospheres were redispersible in solvents such as THF, toluene, or chloroform. Once dried, the semi-shaved hollow nanospheres were essentially insoluble in common organic solvents. This behavior is similar to that of the PCEMA nanospheres prepared from shaving off the PI corona of a PI-*b*-PCEMA star polymer.[9] Due to

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Table 2. Properties of Hairy, Semi-shaved, and Fully Shaved Hollow Nanospheres

sample	solvent	R_h/nm by LS	R_G*/nm by LS	ν/(mL/g)	$\bar{M}_w$*/ (g/mol) by LS
un-cross-linked vesicles	HX/THF (8/2)	56 ± 1^a			
hairy hollow nanospheres	HX/THF (8/2)	54 ± 1^a	39	0.180	2.1×10^8
hairy hollow nanospheres	THF	58^b			
semi-shaved hollow nanospheres	THF	47^b			
fully shaved hollow nanospheres	THF	46^b			

[a] Values averaged over those determined from five scattering angles ranging from 30 to 150°. [b] Values determined at the scattering angle of 90°.

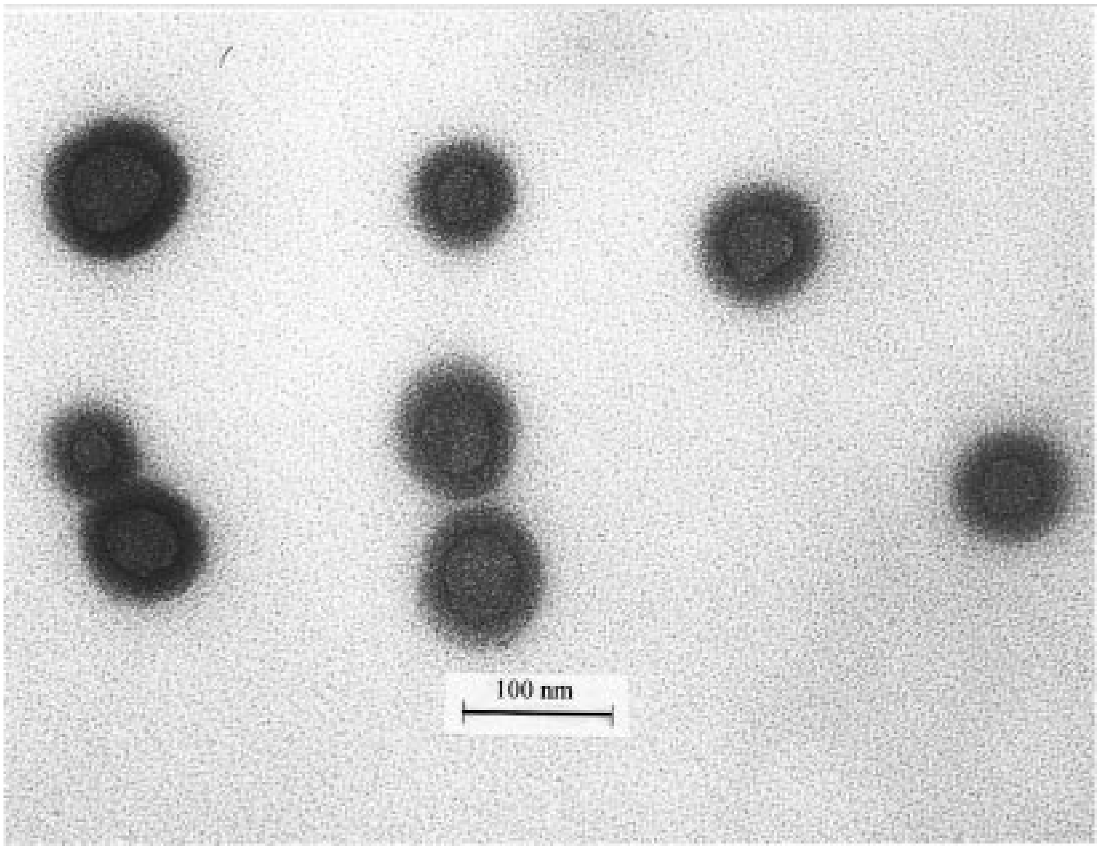
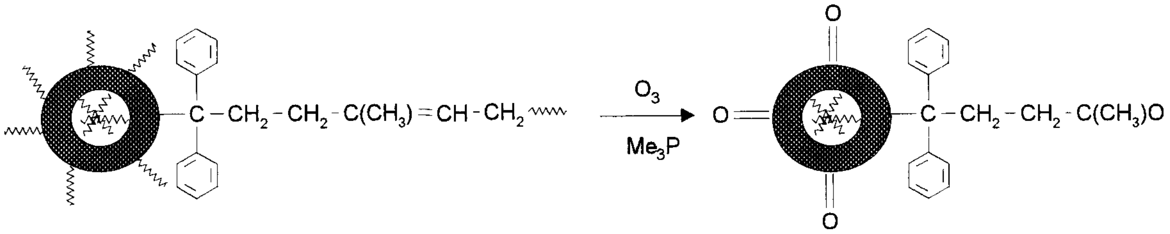


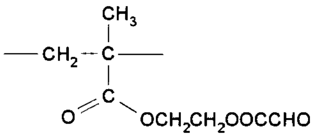
Figure 4. TEM image of the cross-linked PI-*b*-PCEMA vesicles treated with ozone for 0.5 min.

Scheme 1



the poor solubility, we could not carry out static light-scattering studies of the sample.

Ozonolysis of PI and PCEMA. Since isoprene was polymerized in hexane, 93% of the isoprene units were shown to incorporate into the polymer by 4,1-addition.[16] If only the outer PI chains are degraded, the reaction scheme should be as shown in Scheme 1. Or the ozonolysis treatment should have left ketone groups on the hollow-sphere outer surfaces.[16] The degradation of the PCEMA double bonds, which survived UV cross-linking, should yield



$$-CH_2-\overset{\displaystyle CH_3}{\underset{\displaystyle O{=}C{-}OCH_2CH_2OOCCHO}{C}}-$$

Since a carboxyl group is next to the newly formed aldehyde group, it remains to be examined if such a species is stable.

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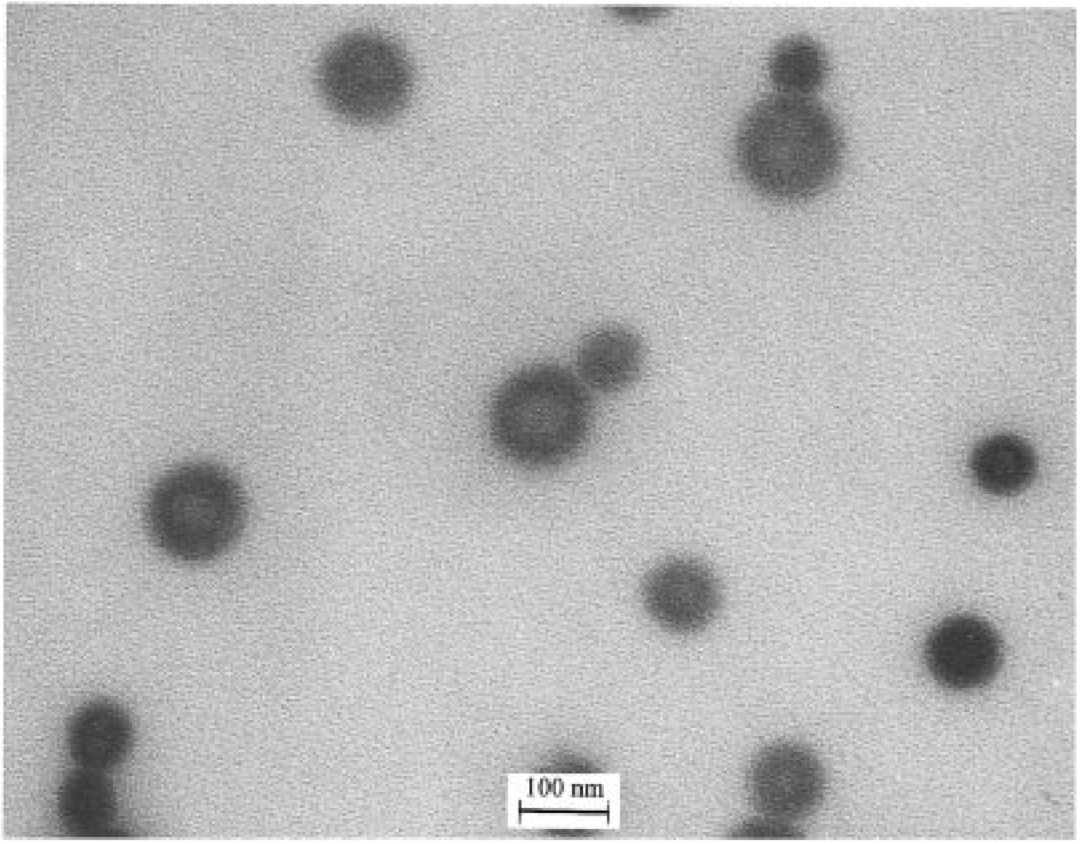

Figure 5. TEM image of the cross-linked PI-*b*-PCEMA vesicles treated with ozone for 10 min.

Fully Shaved Hollow Nanospheres. Illustrated in Figure 5 is a TEM image of a hollow nanosphere sample treated with ozone for 10 min. The disappearance of the dark ring separating the cavity and the PCEMA skeleton suggests the decomposition of the inner PI layer. This is further confirmed by FTIR results shown in Figure 3. The shoulder at 1781 cm^{-1} has increased further in intensity at the further expense of the peak at 1451 cm^{-1}. The R_h value of the fully shaved nanospheres (Table 2) was comparable to that of the semi-shaved nanospheres, as expected.

Like semi-shaved nanospheres, the freshly precipitated fully shaved hollow nanospheres were redispersible in solvents such as THF and chloroform. Once dried, they are even less soluble than the semi-shaved hollow nanospheres in the common organic solvents.

IV. Conclusion

Vesicle formation from a PI-*b*-PCEMA sample in THF/HX mixtures has been confirmed by our TEM results. The PI chains in the vesicles stretched into the solution phase from both the inner and outer PCEMA surfaces. Hairy hollow nanospheres were prepared by photo-cross-linking the PCEMA spherical solid shell or skeleton. The PI chains on the outer surface can be selectively shaved by treating the cross-linked vesicles with ozone for a short period of time. Longer ozone treatment degraded both the outer and the inner PI chains. While ozonolysis was performed here, the general conclusion is that one can perform different chemistry to the different PI chains to generate different functional groups on the inner and outer surfaces. These functionalized hollow nanospheres may be useful as macroporous resins in chemical separations or in controlled drug delivery.

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