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[9] a) **1a**: ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = -2.66$ (s, 2H; imide-NH), 2.57 (d, $J = 4.1$ Hz, 8H; CHCH_2CO$_2$CH$_3$), 3.25, (s, 12H; CHCH$_2$CO$_2$CH_3), 4.49 (m, 4H; PhCH$_2$O$_2$CCHCH$_2$CO$_2$CH$_3$), 4.97 (s, 8H; PhCH_2O$_2$CCHCH$_2$CO$_2$CH$_3$), 6.82 (br, 4H; urea-NH), 7.23–7.35 (m, 24H; benzyl-ArH and *meso*-phenyl-ArH), 7.48 (d, $J = 7.7$ Hz, 4H; *meso*-phenyl-ArH), 7.73 (t, 4H, $J = 8.1$ Hz; *meso*-phenyl-ArH), 7.90 (s, 4H; urea-NH), 8.47 (d, $J = 8.1$ Hz, 4H; *meso*-phenyl-ArH), 8.66 ppm (br, 8H; β-pyrrolic-CH); ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): $\delta =$ 36.84, 49.82, 52.16, 66.98, 116.76, 121.97, 128.53, 128.87, 129.18, 129.91, 131.59, 132.40, 136.49, 140.05, 155.95, 171.50, 171.95 ppm; MALDI-TOF MS: m/z: 1727.8 [MH$^+$];b) **1b**: ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 2.5$ (br, 8H; CHCH_2CO$_2$CH$_3$), 3.24, (s, 12H; CHCH$_2$CO$_2$CH_3), 4.41 (m, 4H; PhCH$_2$O$_2$CCHCH$_2$CO$_2$CH$_3$), 4.95 (s, 8H; PhCH_2O$_2$CCHCH$_2$CO$_2$CH$_3$), 6.78 (br, 4H; urea-NH), 7.22–7.32 (m, 24H; benzyl-ArH and *meso*-phenyl-ArH), 7.49 (s, 4H; urea-NH), 7.58 (d, $J = 6.3$ Hz, 4H; *meso*-phenyl-ArH), 7.71 (t, 4H, $J = 8.0$ Hz; *meso*-phenyl-ArH), 8.39 (d, $J = 8.4$ Hz, 4H; *meso*-phenyl-ArH), 8.61 ppm (dd, $J = 11.6$, 4.5 Hz, 8H; β-pyrrolic-CH); ^{13}C NMR (75 MHz, CDCl$_3$): $\delta = 36.72$, 49.60, 52.17, 67.68, 116.01, 123.23, 123.61, 128.48, 128.78, 128.90, 129.82, 131.96, 132.11, 134.96, 135.41, 139.74, 150.55, 150.64, 155.72, 171.76 ppm; MALDI-TOF MS: m/z: 1790.7 [MH$^+$].

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[11] Compound **1b** does not exist in dimeric or oligomeric forms below $\approx$ 1 mM concentration; this was inferred from the ^{1}H NMR dilution titration of urea-appended porphyrins in CDCl$_3$. In addition, chiral urea-appended porphyrin analogues without carbonyl groups did not exhibit distinct biphasic CD in the Soret region. Therefore, the distinct CD signs do not originate from the exciton coupling between porphyrins. While approximately symmetrical, the shape of the CD spectrum of **1b** is similar to that obtained from the coupling of two porphyrins, and is also similar to induced CD spectra from the coupling of a porphyrin and aspartate C=O groups.[12a] Induced CD spectra from the coupling of a porphyrin and C=O groups do not have to be symmetrical, as revealed by Mizutani et al.[12a] Furthermore, a relatively unsymmetrical shaped biphasic CD spectrum of **1b** was obtained in the high-resolution CD spectrum of **1b**.

[12] Mizutani et al. reported that the intermolecular complex between a porphyrin derivative and dimethyl aspartate exhibited a distinct biphasic CD in the Soret region, and this originated from the coupling between the transition moment of the two carbonyl chromophores of dimethyl aspartate and that of the porphyrin chromophore; a) T. Mizutani, T Murakami, T. Kurahashi, H. Ogoshi, *J. Org. Chem.* **1996**, *61*, 539 – 548; b) T. Mizutani, T. Ema, T. Yoshida, T. Renné, H. Ogoshi, *Inorg. Chem.* **1994**, *33*, 3558 – 3566; c) T. Mizutani, T. Ema, T. Yoshida, Y. Kuroda, H. Ogoshi, *Inorg. Chem.* **1993**, *32*, 2072 – 2077.

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Micelles and Hollow Nanospheres Based on ε-Caprolactone-Containing Polymers in Aqueous Media**

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Motivated by the great range of potential applications, the development of polymeric nanostructures has witnessed great progress in the last decade.[1] Among the target materials, polymeric hollow nanospheres are especially interesting and are in great demand because of their ability to encapsulate large quantities of guest molecules, particularly those with functionalities within the inner cavity.[2] The most studied procedures[3] for preparing polymeric hollow nanospheres from block copolymer precursors involves many steps: preparing micelles in the selective solvents, cross-linking of the micellar corona, and removing the core by chemical degradation. However, further development has been limited by the preparation of block copolymers containing both cross-linkable and degradable blocks.

We have been attempting to produce polymeric micelles in which only hydrogen bonds, rather than covalent bonds, connect the core and shell.[2e,4] As a significant advance in a "block-copolymer-free" strategy for preparing micelles, we

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report here an entirely new approach to the preparation of micelles and hollow spheres through self-assembly of a homopolymer and a random copolymer, both of which are readily attainable. The principle of the procedure is illustrated in Figure 1. The polymer pair of poly(ε-caprolactone) (PCL) and the graftlike copolymer MAF (formed from methylacrylic acid (MAA), macro-monomer FA [CH_2=$CHCOOCH_2$-$CH_2(OCOCH_2CH_2CH_2CH_2CH_2)_3OH$] and methyl methacrylate (MMA), see Experimental Section), which has a hydrophilic backbone and short PCL branches, self-assembles into micelles when a mixture of them in DMF is added to water. The PCL does not precipitate but forms a micellar core that is stabilized by the hydrophilic main chains of MAF, thus forming a shell with the PCL branches anchored to the aggregate. In this new kind of micelle, neither covalent bonds nor hydrogen bonds exist between the core and shell. The affinity between the PCL homopolymer and the short PCL branches is believed to be beneficial to the formation of the micelles. Furthermore, the micelle shell can be cross-linked chemically to form "shell-cross-linked knedel-like nanoparticles" (SCKs),[5] the core of which can be biodegraded by an enzyme to give hollow nanospheres.

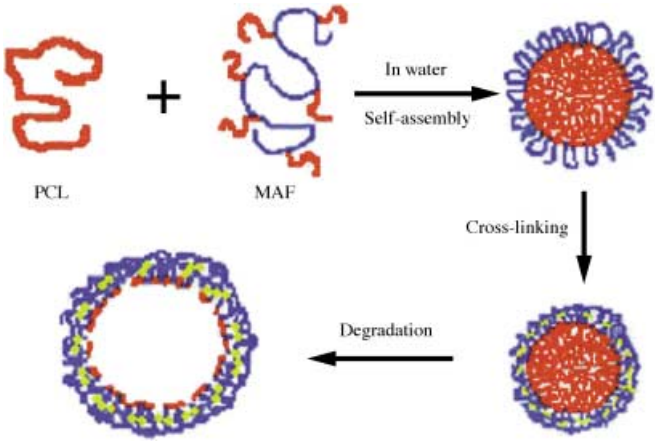

Figure 1. A schematic illustration of the processes of self-assembly, cross-linking, and degradation.

The dependence of micelle size on both the composition of MAF and the ratio of [PCL] to [MAF] was investigated by dynamic laser-light scattering (DLS). In all cases, the particles showed relatively narrow size distributions (size polydispersity ($\mu_2/\langle\Gamma\rangle^2$) was found to be in the range 0.08 to 0.16. The particle size varies considerably, depending on both the MAF and blend compositions, and ranges from 90 to 190 nm (Figure 2). The three series of particles, composed respectively of MAF-1, 2, and 3 (Table 1, see Experimental Section) show a parallel trend that the particle size increases with increasing PCL content for blends in the range of 10 to 50 wt%. This variation is understandable since the PCL aggregates are stabilized by the hydrophilic main chains in MAF. PCL precipitated out when its content exceeded 50 wt%, when the quantity of PCL branches in the MAF is not sufficient to stabilize the PCL aggregates. In addition, the results also show that for any given PCL concentration, the higher the FA content is, the smaller the respective particles

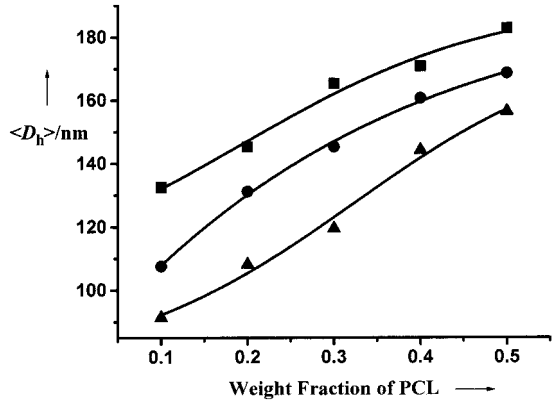

Figure 2. The average hydrodynamic diameter of the micelles of MAF-X/PCL as a function of the weight fraction of PCL. ■: MAF-1, ●: MAF-2>, ▲: MAF-3.

Table 1. The molecular weight and its distribution and T_g of MAF.

Sample no.	Monomer molar ratio[a] MMA/FA/MAA	$M_n \times 10^5$[b]	M_w/M_n[b]	T_g [°C]
MAF-1	9.2/11.8/79.0	5.25	1.78	32.6
MAF-2	6.9/23.8/69.3	3.90	1.60	−27.7
MAF-3	6.1/34.0/59.9	4.16	1.44	−37.1

[a] Measured by ^{1}H NMR spectroscopy. [b] Estimated by size exclusion chromatography in DMF.

are. This observation is also reasonable as an increase in the FA content implies there is a relative increase in the short PCL branches to the homopolymer, which will certainly favor a finer dispersion of PCL aggregates.

DLS measurements show that after cross-linking, the hydrogel displays less swelling than the un-cross-linked shell. For example, for MAF-2/PCL (1:1, w/w), the average hydrodynamic diameter ($\langle D_h\rangle$) varies from 162 to 128.5 nm as a result of cross-linking.

The enzyme lipolase is a type of lipase that can selectively degrade polyesters and fats, hence it was chosen to hydrolyze the polyester core domain without affecting the cross-linked poly(methylacrylicamide) structure of the main chains. Changes in the size and morphology of the SCKs upon hydrolysis of the core were studied by using a combination of DLS and transmission electron microscopy (TEM).

DLS was used to trace the process of core degradation as well as the formation of the hollow spheres. For the micelles of MAF-3/PCL (1:1, w/w), the relative intensity and average hydrodynamic diameter of the micelles of MAF-3/PCL (1:1, w/w, Figure 3) apparently follow opposite trends with reaction time, that is, the intensity gradually decreases with increasing size. This trend actually reflects that the size increase was accompanied by a decrease in the mass as the degradation proceeded. During the initial stage of the reaction (0–100 min) the intensity dramatically decreased, which indicates that an immediate and quick degradation occurs, while no distinct change in the particle size was detected. A significant increase in $\langle D_h\rangle$ from about 110 to 300 nm was observed in the period 400–1200 min, and accompanied by a slow decrease in intensity. In the final stage, neither the intensity nor $\langle D_h\rangle$ changed, which indicated that degradation of the core was

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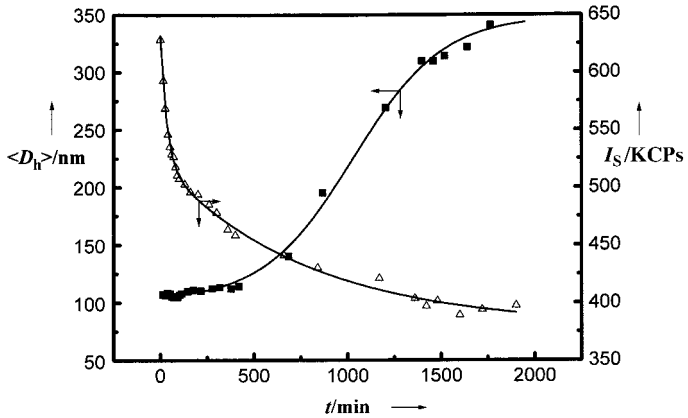

Figure 3. Average hydrodynamic diameter ($\langle D_h \rangle$) and scattering light instensity (I_s, kilo-counts per second) of the micelles MAF-3/PCL (1:1, w/w) at 25 °C as a function of degradation time.

complete. The most remarkable phenomenon, as suggested by DLS data, is the significant increase in micellar diameter from 100 to 350 nm when the mass of the particles was reduced by half. Similar behavior has been previously reported for the micelles of block copolymers on removing species contained within the micellar interior.[3b,4f] This expansion is caused by releasing the restriction imposed by the insoluble blocks on the solvated blocks in the shell. The same phenomenon occurs here, and is indicative of the restriction on the MAF chains caused by the insoluble PCL chains in the core, even though there are no chemical bonds between them. The cross-linked shell, which contains poly(methylacrylamide) segments, can be regarded as a hydrogel that swells more extensively when the core domain fills with water after the removal of the PCL.

The TEM studies gave direct evidence of the morphologies of the micelles and hollow spheres. A typical photograph of the micelles of MAF-2/PCL (1:1, w/w) is shown in Figure 4A in which the micelles clearly display a spherical shape. Figure 4B presents the morphological details of a single micelle at a higher magnification. The micelles have a three-layer structure, with the PCL core being the major constituent of the particle. The gray outer shell is believed to be composed of the hydrophilic main chains of MAF. Interestingly, the inner shell shows much lower chain density, which can be attributed mainly to the short PCL branches. These morphological results illustrate the role of the PCL branches: they act as a "glue" between the outer shell and core by means of the affinity between the PCL homopolymer chains and branches, which are chemically identical. Although the combined thickness of the inner and outer shell is only about 10 nm while the radius of the core is as large as 45 nm, the calculated volume fraction of the shell at 47.7 % is comparable to that of the core, which seems reasonable as the weight ratio of MAF to PCL is about 1:1.

The morphologies of the particles after core degradation are shown in Figure 4C and D, with all of the particles clearly displaying a hollow structure. In comparison with the particles shown in Figure 4A and B, the particles have expanded significantly to about 300 nm in diameter and a shell thickness of up to 100 nm, which is indicative of the swelling of the nanocages after removing the PCL core.

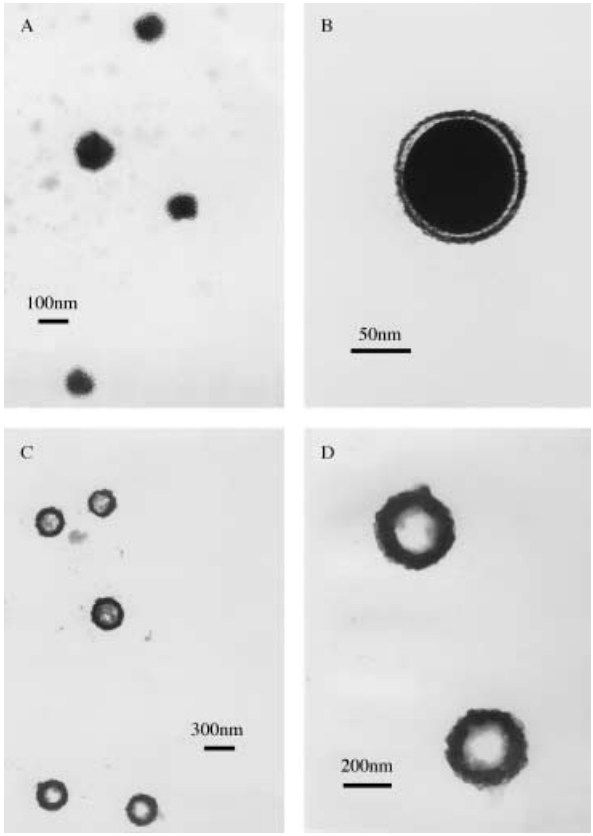

Figure 4. TEM images of MAF-2/PCL (1:1, w/w) nanoparticles before (A and B) and after (C and D) biodegradation.

In conclusion, we have succeeded in obtaining micelles and hollow nanospheres by a "block-copolymer-free strategy". The combination of PCL and MAF led to the formation of micelles possessing a hydrophobic PCL core surrounded by a hydrophilic MAF shell. The central layer, composed of PCL branches in MAF, glues the outer shell to the core. Cross-linking of the micelles gives rise to stable shell-cross-linked nanoparticles. As this route is based on common and nonexpensive polymer products and the processing is simple, it may have great potential for further applications in fabricating supramolecuar materials for various fields such as medicine, catalysis, and photoelectronics.

Experimental Section

A series of the graftlike copolymer MAF was synthesized by free-radical copolymerization of methylacrylic acid (MAA), macro-monomer FA (CH_2=$CHCOOCH_2CH_2(OCOCH_2CH_2CH_2CH_2CH_2)_3OH$, Daicel Chem. Co. Ltd.), and a small amount of methyl methacrylate (MMA) in DMF at 70 °C using 2,2′-azo-bisbutyronitrile as initiator. The products were purified by dissolution–precipitation in DMF/water three times. The copolymers are characterized by a hydrophilic main chain and hydrophobic short PCL branches. Table 1 lists the characterization data of the MAF copolymer prepared with different feed compositions. The copolymer compositions were calculated based on ^{1}H NMR measurements. The signals at $\delta = 0.93$–1.03 for -CH_3 in MAA, $\delta = 1.54$ for $COCH_2CH_2CH_2CH_2CH_2O$ in FA, and $\delta = 3.52$ ppm for -OCH_3 in MMA were used for the calculation. The data show that varying the composition did not significantly affect the molecular weight or the distribution of the copolymers produced under similar reaction conditions. All of the copolymers have a single glass-transition temperature (T_g), which decreases as the quantity of macromer FA increases. This observation indicates

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that there are no highly blocked sequences along the copolymer chains. The micellar nanospheres were prepared by dropwise addition of the various blend solutions of MAF/PCL in DMF into water, with moderate stirring. The appearance of a bluish hue signals the formation of micelles. The mixture was stirred for approximately 24 h at room temperature, and then DMF was removed by dialysis with pure water, which resulted in stable homopolymer/copolymer micelles in water. The micellar structure was locked by cross-linking the hydrophilic shell layer through condensation reactions between the carboxylic acid groups of poly(methylacrylic acid) (PMAA) and the amino groups of hexamethylenediamine in the presence of 1-(3-dimethyl-aminopropyl)-3-ethylcarbdiimide methiodide, which activates the carboxylic acid at room temperature.[3a] The cross-linked product was then dialyzed with distilled water for 3 days to remove the by-products of the reaction. The success of the cross-linking was confirmed by the fact that the resultant nanoparticles maintained their integrity upon switching the medium from water to a solvent mixture containing a large proportion of DMF. DLS (Malven Autosizer-4700) studies on the cross-linked particles found that no particle aggregation had taken place, which meant that there had been almost, zero interparticle cross-linking. For conducting biodegradation of the core, an appropriate amount of dust-free lipolase solution in water (Novozymes Co.) and dilute aqueous NaOH solution was added into the SCK nanoparticulate dispersion.[6] Typical reaction conditions: MAF-3/PCL (1:1, w/w), 50% cross-linked, $C = 2.9 \times 10^{-4}$ g mL^{-1}, pH 8–11 at 25 °C. TEM imaging was performed on a Philips CM 120 electron microscope at an accelerating voltage of 80 kV. The specimens were prepared on copper grids coated with a thin carbon film.

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An Efficient and Highly Enantio- and Diastereoselective Cyclopropanation of Olefins Catalyzed by Schiff-Base Ruthenium(II) Complexes**

Jason A. Miller, Wiechang Jin, and SonBinh T. Nguyen*

Dedicated to Professor Robert H. Grubbs on the occasion of his 60th Birthday

Compounds containing the cyclopropane fragment have received considerable attention because of their frequent occurrence in natural products and their importance as valuable synthetic intermediates.[1–3] Since the introduction of chiral cyclopropanation catalysts by Nozaki et al.,[4] Aratani et al.,[5] and Nakamura et al.,[6] transition-metal-catalyzed asymmetric cyclopropanation has emerged as one of the most efficient synthetic routes to the optically pure cyclopropane fragment.[2,7] Perhaps the most difficult aspect of these asymmetric cyclopropanations is the simultaneous control of yield and regio-, diastereo-, and enantioselectivity while maintaining functional group tolerance.[8,9] In cyclopropanation studies of chiral copper[10–15] and rhodium[16–18] complexes it was found that high enantioselectivities and high diastereoselectivities usually do not go hand-in-hand unless reactions were carried out in an intramolecular manner. Further, in the case of intermolecular cyclopropanation, best enantio- and diastereoselectivities are often only achieved with large diazo esters.

Since the early 1980s, a number of ruthenium complexes have been shown to catalyze olefin cyclopropanation.[1] In view of the advantages that ruthenium-based catalysts have over copper- and rhodium-based catalysts in functional-group tolerance and cost, respectively, the last decade has witnessed an increase in the number of reports on ruthenium-based cylopropanation catalysts, many of which are porphyrin-based.[19–21] Because of the well-known challenges associated with porphyrin synthesis, especially when chiral porphyrins are involved, non-porphyrin multidentate ligands have attracted a lot of attention from investigators over the last few years. In 1994, Nishiyama and co-workers employed a chiral Ru–pybox catalyst (pybox = bis(oxazolinyl)pyridine) for the cyclopropanation of styrene with *tert*-butyl diazoacetate (*t*BDA) and menthyl diazoacetate (MDA) which resulted in high enantio- and *trans*-selectivity.[22–25] However, when the smaller—and more common—diazo ester ethyl diazoacetate (EDA) is employed in this reaction, selectivities are much lower (see Table 1, entry 9). Recently, Katsuki and co-workers

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