Electrochemically Active Block Copolymer Micelles Containing Coumarin Moieties

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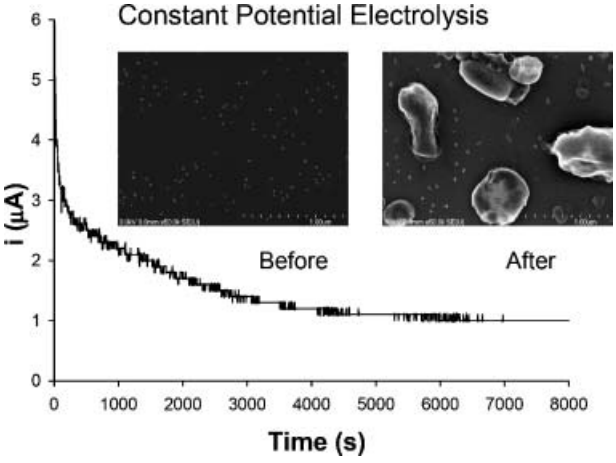
We report the first study of using CPE to disrupt block copolymer micelles containing an organic chromophore. Micelles formed by an amphiphilic diblock copolymer composed of PEO and PCMA are electrochemically active in aqueous electrolyte solution, displaying an irreversible oxidation process of coumarin at a potential of about 1.75 V. CPE of the micellar solution at the fixed oxidation potential allows a large amount of coumarin moieties inside the hydrophobic micelle core to be electrochemically oxidized, resulting in the transformation of small polymer micelles (ca. 38 nm) onto larger aggregates (ca. 1 μm). This study demonstrates that electrochemical redox reactions can be explored as a means to disrupt block copolymers micelles that contain a light-sensitive organic chromophore such as coumarin.



Introduction

Block copolymer micelles are of interest for many possible applications, one of which is drug delivery.[1] Polymer chain self-aggregation due to different solubilities of the blocks in a block-selective solvent is the main driving force for the formation of the micellar aggregates of various morphologies (rods, spheres, vesicles, etc.). In aqueous solution, the hydrophobic block of an amphiphilic block copolymer forms the core of micelle, while the hydrophilic block forms the shell. In the context of drug delivery, poly(ethylene oxide) (PEO) is often used as the hydrophilic block, while a large variety of polymers with specific functionalities can be used as the hydrophobic block.

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Stimuli-responsive polymer micelles are particularly attractive for controlled delivery applications. Their morphology or functionalities can be changed in response to an external stimulus such as pH change,[2] temperature change,[3] sound[4] and light.[5,6] Most research works have been focused on pH- and thermosensitive polymer micelles. In recent years, our group[5] and others[6] have developed light-responsive polymer micelles. However, to our knowledge, there have been only few studies on redox-active or electrochemically active block copolymer micelles, although such micelles formed by small-molecule surfactants have been reported.[7] In the latter case, the most comprehensive studies dealt with micelles containing ferrocene whose electrochemistry is well understood and presents reversible redox activity. Only very recently, the redox-controlled micelle formation and disintegration of block copolymer micelles was reported with the use of an organometallic diblock of polystyrene and poly(ferrocenylsilane) (PFS).[8] PFS has also been used to prepare polyelectrolyte multilayer capsules exhibiting redox-controlled

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permeability and swellability.[9] In both cases, chemical agents were added into the solution for the redox reactions that trigger the changes.

Considering the fact that many photosensitive molecules are also electrochemically active, we anticipated that some photoactive block copolymer micelles might also respond to and be disrupted by the electrochemical stimulus. To test this assumption, we investigated the electrochemical activity of the micelles formed by a diblock copolymer composed of PEO and poly(coumarin methacrylate) (PCMA).[5e] These micelles have the salient feature to be photo-crosslinkable through the dimerization of coumarin moieties and subsequently photo-de-crosslinkable through the cleavage of the dimers (cyclobutane bridges) upon UV irradiations at two different wavelengths (Figure 1).[5e] And as a matter of fact, coumarin is known to display electrochemical activity and can be oxidized by oxidation agents.[10] For instance, Bhavar et al. studied the chemical oxidation of coumarin and its derivatives, and reported the formation of hydroxycoumarin,[11] while Komatsu et al. later conducted a similar study by means of electrochemical oxidation.[12] If our coumarin-based polymer micelles can indeed be disrupted due to their electrochemical activity, the study would confirm the possibility of exploring electrochemical redox reactions as a general means to control photoactive block copolymer micelles.

In this paper we report our study on the coumarin-containing block copolymer micelles using cyclic voltammetry (CV), constant potential electrolysis (CPE), scanning electron microscopy (SEM), ^{1}H NMR, UV-vis and fluorescence spectroscopy. As will be shown, the micelles of poly(ethylene oxide)-*block*-poly(coumarin methacrylate) (PEO-*b*-PCMA) are electrochemically active and can be disrupted by CPE in aqueous solution. To the best of our

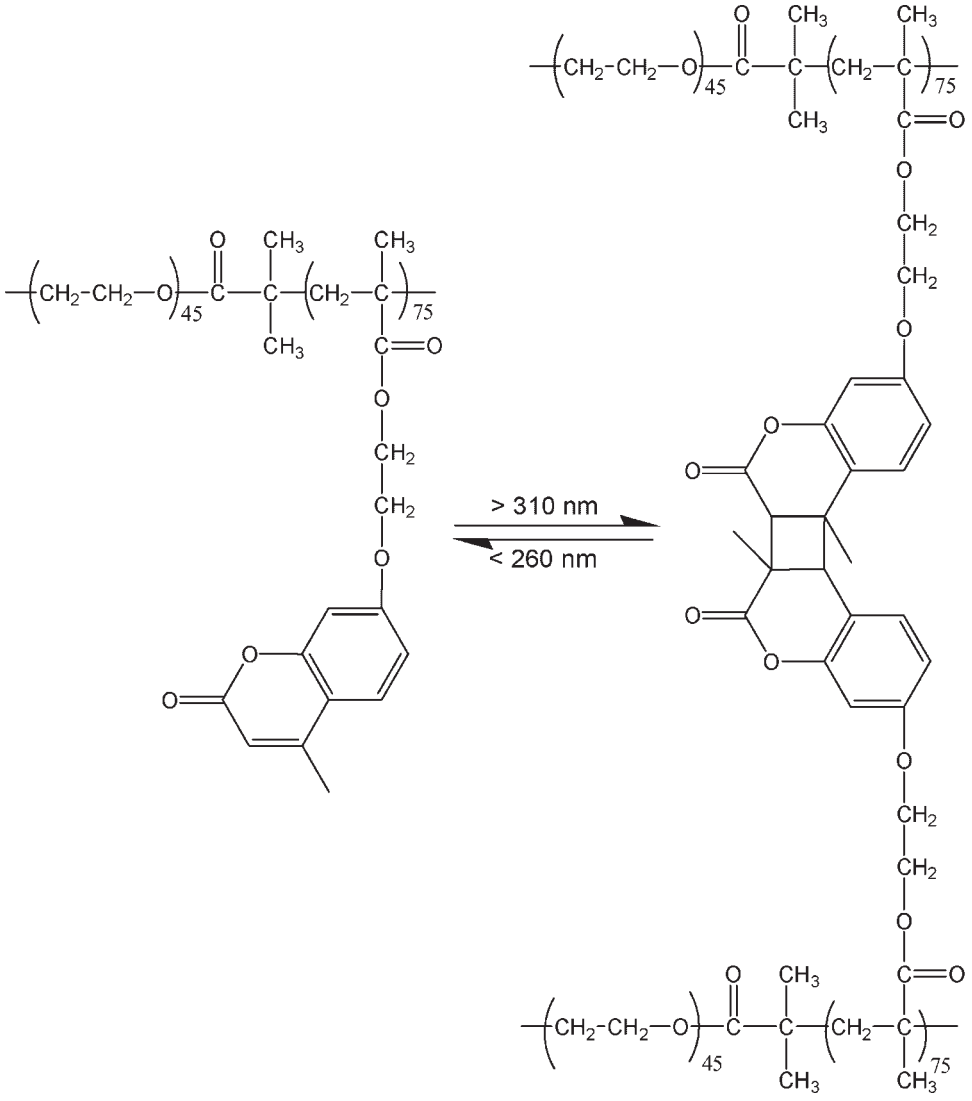

Figure 1. Chemical structure of the diblock copolymer PEO-*b*-PCMA and the reversible photoreactions at different wavelengths.

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knowledge, this is the first report of electrochemically active block copolymer micelles containing an organic chromophore, which differs from the chemical oxidation/reduction of PFS-based organometallic polymer systems.[8,9] And the concept of using redox-active organic chromophores to trigger the release of guest molecules loaded in block copolymer micelles is also different from the electro-release using redox-active polymer-modified electrodes.[13]

Experimental Part

The synthesis and characterization of PEO-*b*-PCMA was reported previously.[5e] The sample used in this study was PEO_{45}-*b*-$PCMA_{75}$, the composition being determined by ^{1}H NMR. Coumarin without substitution was purchased from Aldrich (purity ≥99%). The electrolyte solutions of micelles used for the measurements of CV and CPE were prepared as follows. An aqueous micellar solution was first obtained by slowly adding 25% (v/v) of distilled water into a DMSO solution of the copolymer (1 mg · mL^{-1}, unless otherwise mentioned), which induced the formation of micelles; the micellar solution was then dialyzed against water for 3 d to remove DMSO (dialysis bags from Spectra/Por, cut-off molecular weight: 3 500 Da). Afterwards, 1 mL of the micellar solution was added into 10 mL of a 0.1 M sulfuric acid (H_2SO_4) solution acting as the supporting electrolytes (the polymer concentration mentioned in the discussion refer to the concentration before the dilution by the H_2SO_4 solution). For Nile Red (NR)-loaded micellar solutions, basically the same preparation procedure was utilized. The encapsulation of NR by the micelles was obtained by dissolving both PEO-*b*-PCMA and NR in DMSO (at a concentration of 1 and 0.04 mg · mL^{-1}, respectively). Upon addition of water, polymer micelles were formed while solubilizing NR; precipitated NR was removed by microfiltration. Note that under the used acidic conditions no hydrolysis of coumarin in the micellar solution took place, since no spectral changes of the chromophore were observed without the electrolysis. Likewise, NR-loaded micellar solutions showed no changes in fluorescence emission prior to the electrolysis.

For the electrochemical study, all solutions were deoxygenated by bubbling nitrogen for at least 10 min. All measurements were carried out at room temperature using a potentiostat (Princeton Applied Research, Model 263A). For the CV measurements, a glassy carbon electrode (5 mm in diameter) was used as the working electrode, a Pt wire as the counter electrode and a saturated calomel electrode (SCE) as the reference electrode. The working electrode was first polished with alumina slurry using a Texmet cloth (both the 1-μm alumina particles and the polishing pad were purchased from Buehler) and then sonicated in water prior to each use. The solution was not stirred during the CV measurements. In the case of CPE, the working electrode used was indium-tin-oxide (ITO) in order to have a larger electrode surface. The ITO-coated glass plates (purchased from Delta Technologies) were cut into pieces of 2 × 2 cm and prepared by repeated sonications in distilled water, acetone, chloroform, and distilled water again (5 min for each sonication treatment). During the CPE, the electrolyte solution was constantly stirred using a magnetic stirrer (ca. 80 rpm), and the potential of ITO was maintained at 1.75 V versus SCE using the potentiostat. As will be shown, the potential of 1.75 V corresponds to the oxidation potential of coumarin moieties in the aqueous solution of block copolymer micelles as revealed by the CV measurements.

A number of other characterization techniques were also utilized in this study. UV-vis absorption and steady-state fluorescence emission spectra were recorded using a UV-vis spectrophotometer (Varian 50) and a fluorescence spectrophotometer (Varian), respectively. The excitation wavelength was 330 nm for coumarin groups and 555 nm for Nile Red (excitation and emission slit widths were set at 5 nm, and the scan rate was 10 nm · s^{-1}). The photo-crosslinking of polymer micelles was achieved by exposing the micellar solution to UV light at wavelengths >310 nm generated from a UV-vis spot curing system (Novacure) operating with a 320–400 bandpass filter. ^{1}H NMR spectra were obtained using a Bruker Spectrometer (300 MHz, AC 300). SEM observations were made on a Hitachi S-4700 Field-Emission-Gun SEM operating at 3 kV. The samples for SEM were prepared by casting a drop of the micellar solution, either before or after electrolysis, on a silicon wafer (purchased from Motorola, type N, cut into pieces of 0.5 mm × 0.5 mm), followed by drying at room temperature.

Results and Discussion

Figure 2 shows the CV curves of the micellar solution of PEO-*b*-PCMA at three different polymer concentrations and, for comparison, the electrolytic solution without the copolymer (scan rate 10 mV · s^{-1}). The micellar solution presents an oxidation peak around 1.75 V, which is absent in the electrolyte solution without micelles. However, the process is irreversible, since no reduction peak is observed in the potential range studied and no current goes into cathode part. As the polymer concentration is increased, the peak current increases from about 300 μA (0.5 mg · mL^{-1})

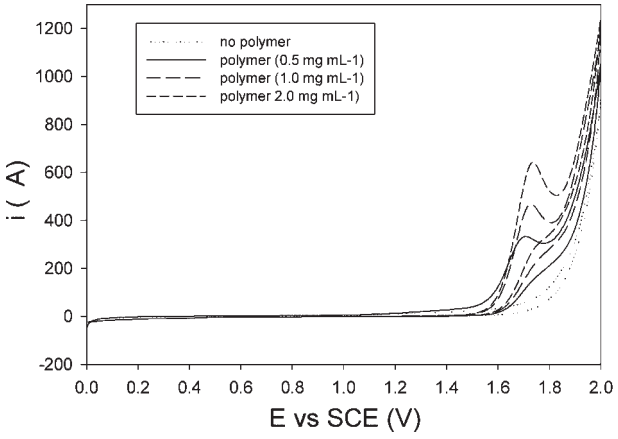

Figure 2. CV curves for micellar solutions with different polymer concentrations (0.5, 1.0 and 2.0 mg · mL^{-1}) and for the electrolyte solution without polymer. The scan rate is 10 mV · s^{-1}.

to 600 μA (2 mg · mL^{-1}), indicating that more coumarin moieties are oxidized upon each CV scan. A shift of the oxidation potential into the positive direction can also be noticed with increasing the polymer concentration (ca. 40 mV). This change is related to the uncompensated drop in IR in solution (current intensity × resistance) with increase of the peak current. To get more insight into the oxidation behavior of the polymer micelles, we carried out additional measurements. In Figure 3 the CV curves of the micellar solution with 1 mg · mL^{-1} of PEO-*b*-PCMA subjected to different scan rates ranging from 1 to 200 mV · s^{-1} are compared. The oxidation potential of the micelles is steadily increased from 1.70 V to 1.81V with increasing the scan rate. The inset is the plot of the peak current, i_p, versus the square root of the scan rate, $v^{\frac{1}{2}}$; the straight line indicates that the oxidation of polymer micelles is a diffusion-controlled irreversible process.

An interesting difference is observable between the oxidation of the small-molecule coumarin without substitution ($C_9H_6O_2$) and the coumarin moieties on the block copolymer micelles. In the case of coumarin, after one CV scan, the oxidation peak is severely reduced, while after two scans no peak can be observed (Figure 4a). This implies that oxidized coumarin molecules could adhere to the surface of the electrode, which blocks the electrode surface and thus prevents coumarin molecules in solution from being oxidized upon subsequent scans. By contrast, with polymer micelles where coumarin moieties are confined in the hydrophobic core of PCMA, repeated scans (up to 15 times) only results in a very slight decrease in the peak current (only 5 scans are shown in Figure 4b for the sake of clarity). This result suggests that upon each scan, oxidized coumarin moieties remain inside the micelles; the PEO shell prevents oxidation products from being adsorbed on the electrode surface. In other words, oxidized polymer micelles are free to diffuse into the bulk solution and leave the electrode accessible to other micelles for their oxidation. For the CV measurements of coumarin, the compound, being insoluble in water, was first dissolved in a mixture of methanol/water (7/5, v/v) before adding the same supporting electrolyte as for the polymer solution.

Now, what is the effect of the electrochemical oxidation of coumarin moieties on the block copolymer micelles? No UV-vis and fluorescence spectral changes of the micellar solution were observed even after 15 consecutive CV scans. This may be understood by the fact that only a very small

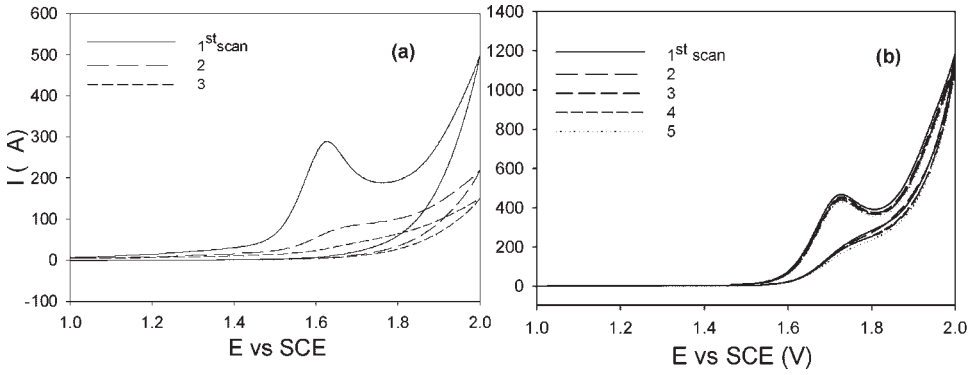

Figure 4. CV curves for (a) coumarin (9 × 10^{-3} mol · L^{-1}) over three consecutive scans, and (b) a polymer micellar solution (1 mg · mL^{-1}) over five consecutive scans. Scan rate is 10 mV · s^{-1}.

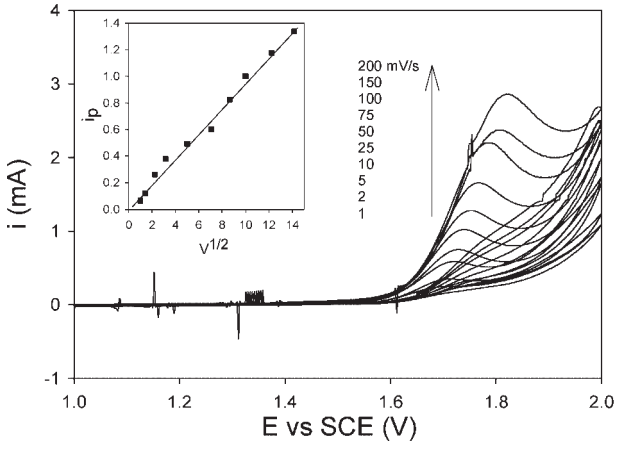

Figure 3. CV curves for a polymer micellar solution (1 mg · mL^{-1}) subjected to different scan rates. Inset shows the plot of the peak current versus the square root of the scan rate.

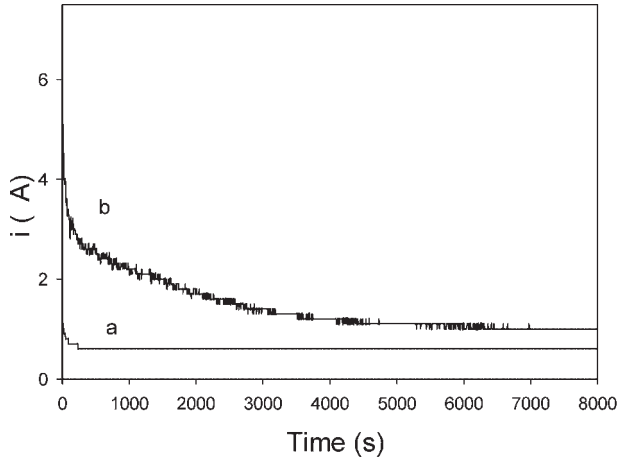

Figure 5. CPE curves for a) the electrolyte solution without polymer and b) the polymer micellar solution (1 mg mL^{-1}), the potential being fixed at 1.75 V.

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fraction of micelles, i. e., those close to the electrode, get actually oxidized upon each scan. In order to know whether or not the micelles of PEO-*b*-PCMA can be disrupted by the electrochemical oxidation of coumarin, we then used the controlled potential electrolysis (CPE) method, by fixing the potential of the ITO working electrode at 1.75 V which corresponds to the oxidation potential of the coumarin-containing polymer micelles.

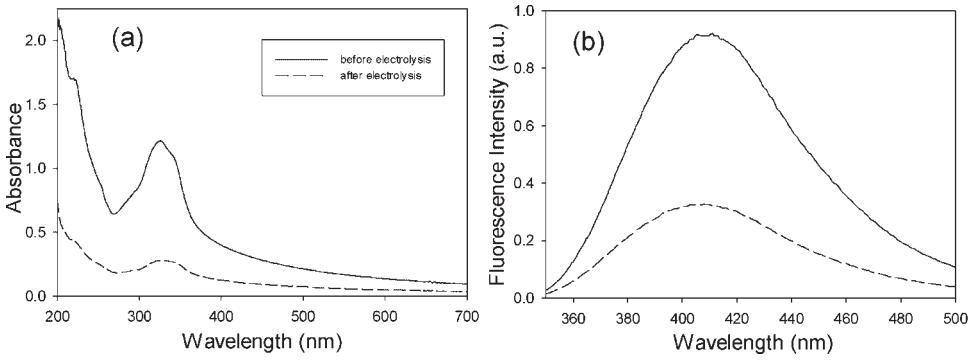

Figure 6. (a) Absorption and (b) fluorescence emission ($\lambda_{ex} = 330$ nm) spectra of the polymer micellar solution before and after the electrolysis.

Figure 5 shows the typical current vs. time transient, for the micellar solution (1 mg · mL^{-1} polymer) and, for comparison, the electrolyte solution without polymer micelles. While the electrolyte solution alone shows small and quickly diminishing residual current, the micellar solution is clearly more active due to the oxidation of coumarin moieties. The electro-activity decreases with time, most of the oxidation of coumarin groups in the micelles appears to take place within the first 50 min, after which some residual constant current is still observed. This residual activity probably arises from the remaining coumarin moieties, the oxidation of which might be hindered by the electrolysis- induced structural rearrangements inside the micelles. Knowing the polymer concentration in the electrolyte solution and assuming that the oxidation is a one-electron process, the integration of the current-time transient[14] in Figure 5 yielded an estimated 92% of coumarin moieties oxidized after 8 000 s. Note that the CPE measurements were carried out with the solution stirred with a stirrer at the bottom of the cell, which caused some current noise. When the polymer micellar solution was subjected to fixed potentials below the oxidation peak value, e.g. 1 V, no electro-activity was observed.

In contrast to the little effect of CV scans, the electrolysis at the fixed oxidation potential of coumarin moieties allows the electrochemical process to develop in time throughout the micellar solution (volume effect). Figure 6 shows the absorption and fluorescence emission spectra of the electrolyzed micellar solution recorded after 8 000 s of CPE. The drop of the absorption of coumarin moieties around 320 nm indicates that most (ca. 75%) of them are affected by the electrochemical oxidation (Figure 6a). The fluorescence intensity of coumarin moieties at around 410 nm is also reduced by about 70% after the electrolysis (Figure 6b), while a blue shift of ca. 7 nm for the emission maximum can be noticed. These results show that the micelles of PEO-*b*-PCMA can be disrupted by the solution electrolysis. However, it should be emphasized that the decrease in absorption and fluorescence emission of coumarin cannot be quantitatively related to the estimated degree of electrolysis, because they depend on the aggregation states and the environment of the chromophore. What is safe to say is that the spectral changes of the electrolyzed micellar solution are consistent with the electrochemical oxidation of coumarin moieties evidenced by the CPE result (Figure 5). Moreover, the decrease of the UV-vis spectral baseline agrees with the observable increase in optical transparency of the electrolyzed micellar solution, which is accompanied by the suspension and precipitation of larger aggregates. We thus measured the change in turbidity of the micellar solution as a function of the electrolysis time. The turbidity τ was calculated according to $\tau = 2.3\ A/L$,[15] where A is the absorbance at $\lambda = 600$ nm and L is optical path length ($L = 1$ cm, which is the width of the cuvette). The wavelength of 600 nm was used because it is far from the absorption of the micelles. The result in Figure 7 shows that the turbidity decreases quickly within the first hour and the decrease becomes

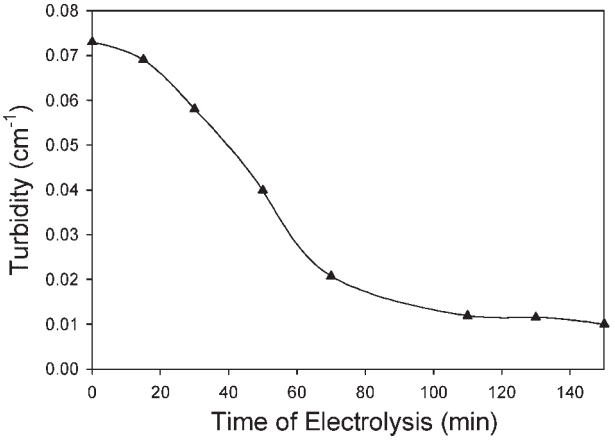

Figure 7. Change in turbidity of the polymer micellar solution (measured at 600 nm) as a function of the electrolysis time.

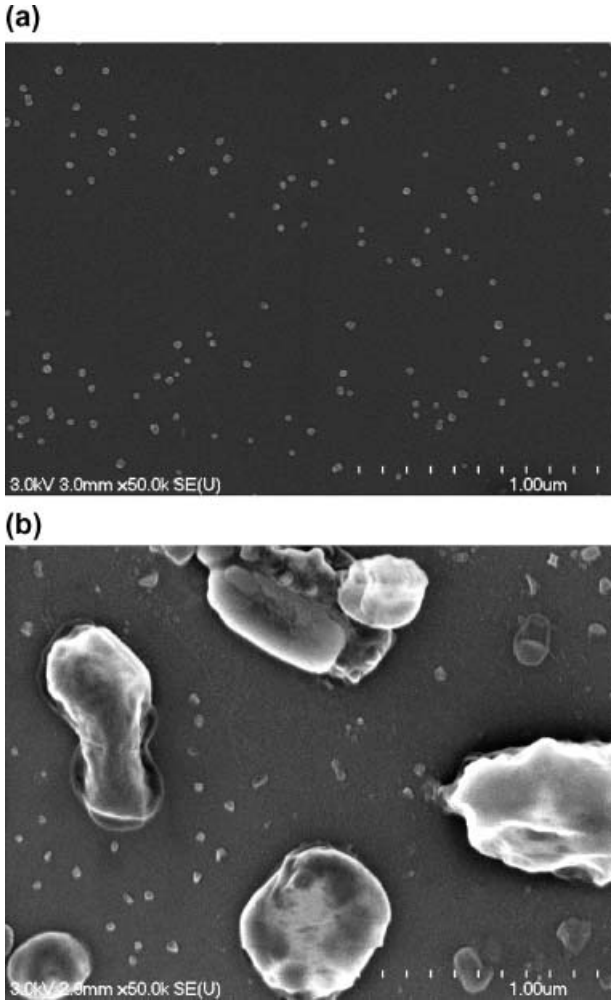

Figure 8. SEM images of the polymer micellar solution cast on silicon wafer, (a) before and (b) after the electrolysis, showing the disruption of polymer micelles. The scale bar on the pictures is 1 μm.

more slowly at longer times. The change indicates the disruption of polymer micelles upon electrolysis. As shown in Figure 8, SEM observation on the micellar solution before and after the electrolysis confirms the disruption of polymer micelles, resulting in the formation of much larger aggregates (ca. 0.5–1 μm) that coexist with the remained, apparently unaffected polymer micelles with sizes ranging from 33 to 50 nm (average size ca. 38 nm).

Due to the formation of larger aggregates upon the electrolysis, some of which precipitate onto the bottom of the cell, the changes in absorption and emission intensities of the electrolyzed micellar solutions (Figure 6) provide little information on the possible structural changes of the coumarin-containing polymer. The only meaningful change after the electrolysis is the blue shift of the emission maximum, which is sensitive to structural variations of the chromophore. In an attempt to know if there could be a link between the photoreaction of coumarin moieties, i.e., their dimerization upon UV absorption, and the electrochemical oxidation, we partially photo-crosslinked the micellar solution and recorded the absorption and emission spectra before and after the photoreaction (Figure 9). The photoinduced dimerization of the coumarin moieties can be seen from the decrease in their absorption at 320 nm. Surprisingly, the fluorescence emission of the photolyzed micellar solution also displays a blue shift of ca. 7 nm, the same shift as the micellar solution after the electrolysis (Figure 6b). But at this time, we have no evidence to suggest that the electrolysis of the micelles results in some dimerization of coumarin moieties.

In addition to the above comparative test with the photo-crosslinked micelles, we performed more experiments in order to have better knowledge on the electrochemically oxidized PEO-*b*-PCMA micelles. While the oxidation of coumarin without substitution could result in the formation of hydroxyl radicals of coumarin,[12] the case of the polymer micelles seems to be more complex. The large precipitated aggregates, formed after the electrolysis of the micellar solution, were collected and characterized. They were recovered through separation from the solution, followed by removing the entrapped electrolytes (salts) through dialysis against water, and drying by means of lyophilization. The first indication of structural changes is that the precipitate is soluble in THF, unlike the block copolymer. Figure 10 shows the absorption and fluorescence emission spectra of the precipitate in THF (Figure 10a) as well as its ^{1}H NMR spectrum in DMSO, in comparison with the block copolymer (Figure 10b).

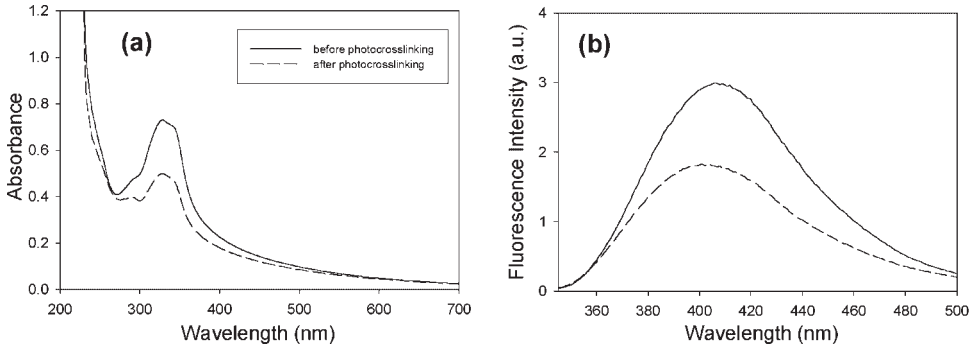

Figure 9. (a) Absorption and (b) fluorescence emission ($\lambda_{ex} = 330$ nm) spectra of a polymer micellar solution before and after partial photo-crosslinking of the micelles through the photo-dimerization of coumarin moieties (indicated by the decrease in absorption around 320 nm).

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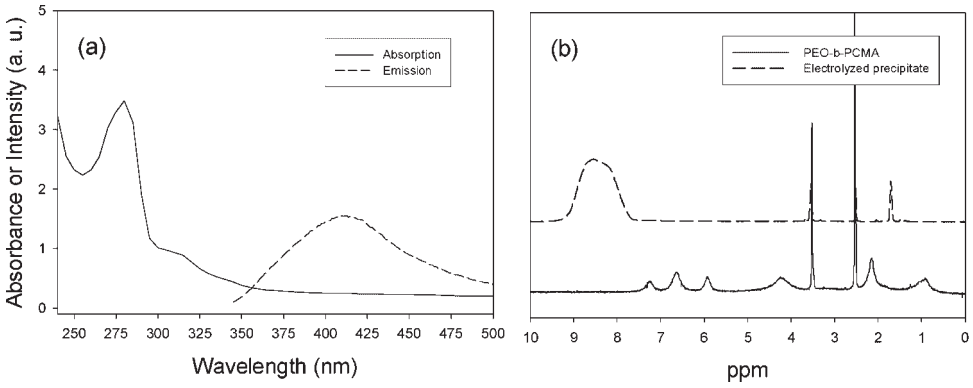

Figure 10. (a) Absorption and fluorescence emission ($\lambda_{ex} = 330$ nm) spectra of the precipitate dissolved in THF, and (b) ^{1}H NMR spectra of the precipitate and the non-electrolyzed PEO_{45}-*b*-$PCMA_{75}$ diblock copolymer in DMSO.

While the non-electrolyzed PEO-*b*-PCMA displays the dominant absorption of coumarin moieties around 320 nm (Figure 6), the precipitate has its main absorption shifted to about 280 nm, with a small but noticeable absorption peak of coumarin remained. This result clearly indicates the structural changes of coumarin moieties caused by the electrochemical oxidation, resulting in the formation of aromatic compounds that usually absorb in the 280 nm region. The fluorescence emission of the precipitate should come from the remaining coumarin groups. The ^{1}H NMR spectrum of the precipitate also displays drastic changes with respect to the non-electrolyzed PEO-*b*-PCMA. Among other things, a broad aromatic proton peak appearing at 7.5–9 ppm replaces the signals of aromatic coumarin in the 5.8–7.5 ppm region. The broad peak suggests that the electrolysis of the coumarin moieties may lead to the formation of various aromatic compounds whose proton signals overlap. The identification of these structures requires future investigations. Another observation hints for the reason of precipitation upon electrolysis. The ratio of the integral of all aromatic proton peaks to the integral of the PEO peak at ca. 3.5 ppm changed from 1.6 for PEO-*b*-PCMA to 25 for the precipitate (the integrals are not shown in Figure 10 for the sake of clarity). This implies that the proportion of the (electrolyzed) PCMA blocks in the precipitate is much more important than in the diblock copolymer. This might be accounted for by one possible event accompanying the electrochemical oxidation of the micelles. It is possible that some ester linkages between the PEO and PCMA blocks (Figure 1), which are introduced by the initiator used for the synthesis of PEO-*b*-PCMA through the atom transfer radical polymerization (ATRP),[5e] could be broken by the electrolysis. Such cleaved hydrophobic polymer chains would favor the precipitation in aqueous solution. However, we emphasize that this is only a possible contribution to the micelle disruption, while the whole of the results suggest that the electrolysis of coumarin groups was the main cause. As pointed out earlier, upon CPE of the micellar solution, both the electro-activity arising from coumarin groups (Figure 5) and the change in turbidity related to changes in micellar aggregates (Figure 7) took place mainly during the first hour of electrolysis. Moreover, we carried out similar experiments with micellar solutions prepared using two other amphiphilic diblock copolymers composed of PEO and either a pyrene- or 2-nitrobenzene-containing poly(methacrylate). In both cases, no electro-activity and no disruption of polymer micelles like with PEO-*b*-PCMA were observed, while these two block copolymers were also synthesized using Atom Transfer Radical Polymerization (ATRP)[5c,5d] and contain the ester linkage between PEO and the hydrophobic polymer block.

Finally, we wanted to know how the disruption of the PEO-*b*-PCM micelles upon electrolysis could affect the encapsulation of a hydrophobic compound. NR is a hydrophobic dye that can be solubilized by the polymer micelles, and its release into aqueous solution can be monitored through the measurement of its fluorescence emission.[5d] We prepared a NR-loaded micellar solution of PEO-*b*-PCMA, and subjected it to CPE under the same conditions as those used for CPE of the unloaded polymer micellar solutions (Figure 5). Figure 11 presents the fluorescence emission spectra of NR ($\lambda_{ex} = 555$ nm) recorded after various times of electrolysis (the chemical structure of NR is also shown). The emission intensity of NR indeed decreases with increasing the electrolysis time. The large change after the first 20 min is consistent with the faster electrolysis of the micelles at the beginning of the process (Figure 5 and Figure 7). However, we are unable to tell if the decrease is mainly due to the precipitate that could entrap NR molecules that are not sampled in recording the emission spectra for the reason mentioned earlier. Nevertheless, one change seems to be significant. With increasing the electrolysis time, in addition to the decreased intensity, a red-shifted emission maximum (by ac. 25 nm) becomes more and more prominent. It is known that in water, the much-quenched fluorescence of NR emits at longer wavelength. This result may be indicative that upon the electrolysis, the disruption of the polymer micelles brings part of NR molecules to a more aqueous medium. Even though some direct electrolysis of NR cannot be totally ruled out, it is unlikely to occur. Under the used conditions, no redox peaks were found for NR dissolved in dichloromethane.

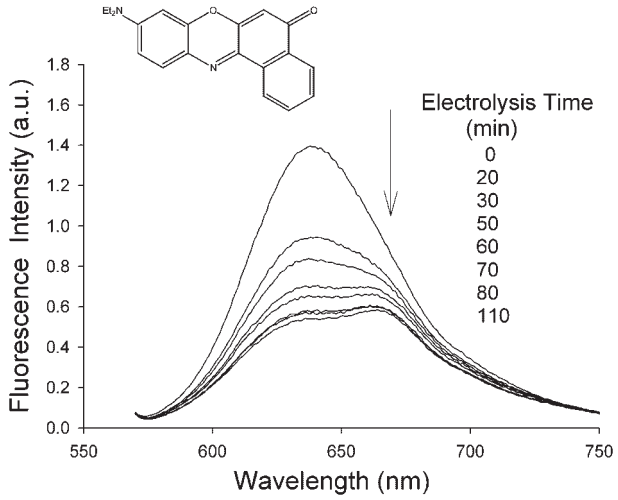

Figure 11. Fluorescence emission spectra of NR ($\lambda_{ex} = 555$ nm) loaded in a polymer micellar solution (1 mg · mL^{-1}) recorded at different times of electrolysis. Chemical structure of NR is shown.

Conclusion

Micelles of the photoactive block copolymer of PEO-*b*-PCMA are also electrochemically active, arising from the oxidation of coumarin moieties at a potential of about 1.75 V. The CV measurements confirmed that the electrochemical oxidation of polymer micelles, with coumarin groups confined in the PCMA core surrounded by the PEO shell, is a diffusion-controlled irreversible process, and that consecutive CV scans only result in very slight change of the oxidation peak, in contrast to small-molecule coumarin. Moreover, the micelles of PEO-*b*-PCMA can be disrupted by electrolysis of the solution subjected to a fixed oxidation potential of the chromophore, which destabilizes a fraction of the micelles (ca. 38 nm) and results in the formation of some larger polymer aggregates (ca. 1 μm). The characterization results suggest that the electrochemical oxidation of PEO-*b*-PCMA might lead to the formation of various aromatic compounds, and that the electrolysis might also break the ester linkages between the PEO and PCMA blocks. The electrolysis-induced disruption of the block copolymer micelles could leave encapsulated hydrophobic NR in a more aqueous medium. This study demonstrates the interest of exploring the electrochemical activity of light-sensitive polymer micelles containing an organic chromophore.

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[1] See, for example, [1a] D. E. Discher, A. Eisenberg, *Science* **2002**, *297*, 967; [1b] R. Haag, *Angew. Chem. Int. Ed.* **2004**, *43*, 278; [1c] V. P. Torchilin, *Adv. Drug Delivery Rev.* **1995**, *16*, 295.
[2] See, for example, [2a] E. R. Gillies, J. M. J. Frechet, *Chem. Commun.* **2003**, 1640; [2b] E. G. Bellomo, M. D. Wyrsta, L. Pakstis, D. J. Pochan, T. J. Deming, *Nat. Mater.* **2004**, *3*, 244; [2c] Y. Bae, S. Fukushima, A. Harada, K. Kataoka, *Angew. Chem. Int. Ed.* **2003**, *42*, 4640.
[3] [3a] J. E. Chung, M. Yokoyama, T. Okano, *J. Controlled Release* **2000**, *65*, 93; [3b] C. M. Schilli, M. Zhang, E. Rizzardo, S. H. Thang, Y. K. Chong, K. Edwards, G. Karlsson, A. H. E. Muller, *Macromolecules* **2004**, *37*, 7861.
[4] N. Rapoport, W. G. Pitt, H. Sun, J. L. Nelson, *J. Controlled Release* **2003**, *91*, 85.
[5] [5a] G. Wang, X. Tong, Y. Zhao, *Macromolecules* **2004**, *37*, 8911; [5b] X. Tong, G. Wang, A. Soldera, Y. Zhao, *J. Phys. Chem. B* **2005**, *109*, 20281; [5c] J. Jiang, X. Tong, Y. Zhao, *J. Am. Chem. Soc.* **2005**, *127*, 8290; [5d] J. Jiang, X. Tong, D. Morris, Y. Zhao, *Macromolecules* **2006**, *39*, 4633; [5e] J. Jiang, B. Qi, M. Lepage, Y. Zhao, *Macromolecules* **2007**, *40*, 790; [5f] B. Qi, Y. Zhao, *Langmuir* **2007**, *23*, 5746; [5g] Y. Zhao, *Chem. Rec.* **2007**, *7*, 286.
[6] [6a] X. Liu, M. Jiang, *Angew. Chem. Int. Ed.* **2006**, *45*, 3846; [6b] H. Lee, W. Wu, J. K. Oh, L. Mueller, G. Sherwood, L. Peteanu, T. Kowalewski, K. Matyjaszewski, *Angew. Chem. Int. Ed.* **2007**, *46*, 2453.
[7] [7a] A. Baran Mandal, *Langmuir* **1993**, *9*, 1932; [7b] T. Saji, K. Hoshino, S. Aoyagui, *J. Am. Chem. Soc.* **1985**, *107*, 6865; [7c] P. Yeh, T. Kuwana, *Electrochem. Sci. Technol.* **1976**, *123*, 1334; [7d] Y. Takeoka, T. Aoki, K. Sanui, N. Ogata, M. Yokoyama, T. Okano, Y. Sakurai, M. Watanabe, *J. Controlled Release* **1995**, *33*, 79.
[8] D. A. Rider, M. Winnik, I. Manners, *Chem. Commun.* **2007**, 4483.
[9] Y. Ma, W.-F. Dong, M. A. Hemipenius, H. Mohwald, G. J. Vansco, *Nat. Mater.* **2006**, *5*, 724.
[10] [10a] Q. Wu, H. D. Dewald, *Electroanalysis* **2001**, *13*, 45; [10b] K. Kim, H. J. Chun, S. O. Paik, S. W. Park, *Anal. Sci. Technol.* **1995**, 655.
[11] M. D. Bhavsar, R. D. Desai, *Indian J. Pharm.* **1951**, *13*, 200.
[12] M. Komatsu, T. N. Rao, A. Fujishima, *Chem. Lett.* **2003**, *32*, 396.
[13] [13a] L. L. Miller, A. N. Lau, E. K. Miller, *J. Am. Chem. Soc.* **1982**, *104*, 5242; [13b] A. N. Lau, L. L. Miller, *J. Am. Chem. Soc.* **1983**, *105*, 5271.
[14] A. Kunai, E. Toyoda, T. Kawakami, M. Ishikawa, *Organometallics* **1992**, *11*, 2899.
[15] J. Narayanan, J. Y. Xiong, X. Y. Liu, *J. Phys.: Conf. Ser.* **2006**, *28*, 83.

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