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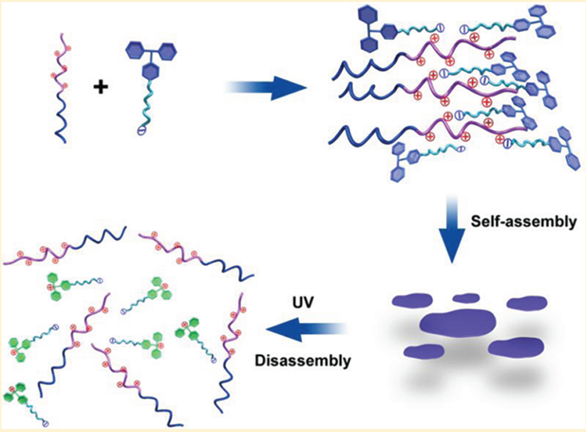
UV-Responsive Polymeric Superamphiphile Based on a Complex of Malachite Green Derivative and a Double Hydrophilic Block Copolymer

Peng Han,[†] Sichao Li,[†] Chao Wang,[†] Huaping Xu,[†] Zhiqiang Wang,[†] Xi Zhang,[*,†] Joice Thomas,[‡] and Mario Smet[‡]

[†]Key Lab of Organic Optoelectronics and Molecular Engineering, Department of Chemistry, Tsinghua University, Beijing 100084, People's Republic of China

[‡]Molecular Design and Synthesis, Catholic University of Leuven, Celestijnenlaan 200F, Box 2404, B-3001 Leuven, Belgium

ABSTRACT: We have prepared a UV-responsive polymeric superamphiphile, formed by a malachite green derivative and the double hydrophilic block copolymer methoxy-poly(ethylene glycol)$_{114}$-*block*-poly(L-lysine hydrochloride)$_{200}$ (PEG-*b*-PLKC) on the basis of electrostatic interactions. The malachite green derivative undergoes photo-ionization upon UV irradiation, which makes it more hydrophilic, resulting in changes in the self-assembly behavior of the polymeric superamphiphile. For this reason, the polymeric superamphiphile originally self-assembles to form sheetlike aggregates, which disassemble after UV irradiation because of the increased solubility of the malachite green derivative. By use of Nile red as a probe, the polarity of the polymeric superamphiphile solution is confirmed to be increased after UV irradiation by fluorescence spectra, which also explains the disassembly of the polymeric superamphiphile.



INTRODUCTION

Amphiphiles are able to self-assemble to form well-defined nanostructures in aqueous solution, which can be applied in many fields such as template synthesis[1] and drug delivery.[2] Compared to conventional amphiphiles, superamphiphiles refer to amphiphiles that are formed by noncovalent interactions instead of covalent bonds.[3] Different noncovalent interactions, such as hydrogen bonding,[4] electrostatic interaction,[5] charge-transfer interaction,[6] host−guest recognition,[7] and so on have been employed to fabricate superamphiphiles with diversified topologies like single chain, double chain, bolaform, gemini, and rotaxane types. When a superamphiphile based on polymers is fabricated, polymeric superamphiphiles can be obtained. For example, double hydrophilic block copolymers with a charged block can attract small molecules with opposite charge, thus forming an amphiphilic complex that can be called a polymeric superamphiphile.[8] The noncovalent preparation of the polymeric superamphiphile avoids complicated synthesis and the use of organic solvents during the micellization when compared with conventional amphiphilic block copolymers. Due to the different functionalities of the employed building blocks, superamphiphiles allow for tuning of their amphiphilicity by external stimuli, leading to controlled self-assembly and disassembly. For polymeric superamphiphiles, different responsive small molecules can be introduced to tune the amphiphilicity of the complex by external stimuli. In our previous work, we have introduced light-responsive, oxidation-responsive, and enzyme-responsive molecules into polymeric superamphiphiles.[9] These superamphiphiles can self-assemble to form well-defined nanostructures like vesicles and micelles and can disassemble upon a certain stimulus because of the increased solubility or degradation of small molecules.

Among all the stimuli, light is one of the most attractive for rapid and clean control of solution properties with specific direction and position. Malachite green, a dye with triphenylmethane structure, is a well-known photochromic molecule and has received considerable attention in both fundamental and applied research.[10] Herein, we report the fabrication of a UV-responsive polymeric superamphiphile formed by an anionic malachite green derivative and a cationic block copolymer, as shown in Scheme 1. The polymeric superamphiphiles self-assemble to form sheetlike aggregates and disassemble after UV irradiation because of the increased solubility of the malachite green derivative. It is anticipated that this work will improve and enrich our understanding of the self-assembly and disassembly of superamphiphiles.

EXPERIMENTAL SECTION

Materials. The block copolymer methoxy-poly(ethylene glycol)$_{114}$-*block*-poly(L-lysine hydrochloride)$_{200}$ (PEG-*b*-PLKC) was purchased from Alamanda Polymers. Nile red was purchased from Sigma−Aldrich. 3-Bromopropane-1-sulfonic acid was also obtained from Sigma−Aldrich.

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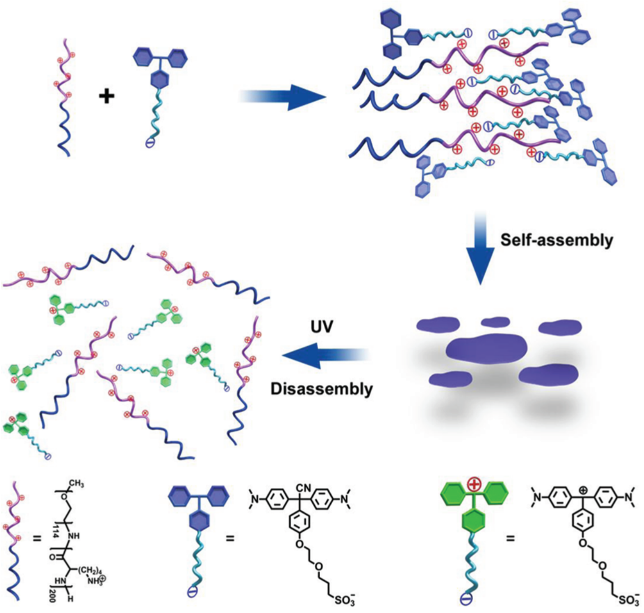
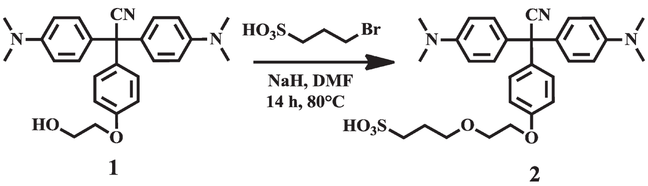
Synthesis of Malachite Green Derivative (MG, 2). Alcohol **1**[10d] (100 mg, 0.24 mmol) and 3-bromopropane-1-sulfonic acid (97 mg, 0.48 mmol) were dissolved in dry *N*,*N*-dimethylformamide (DMF; 8 mL) under argon atmosphere. NaH (60 mg of a 60% dispersion in mineral oil, 2.4 mmol) was added and the resulting suspension was stirred for 14 h at 80 °C. After this, the mixture was evaporated to dryness. The reaction mixture was quenched with ice water (20 mL) and extracted with CH_2Cl_2 (5 × 30 mL), dried over $MgSO_4$, filtered, and evaporated to dryness to afford the crude product . Purification by column chromatography (silica, eluent CH_2Cl_2—MeOH 9:1) afforded **2** (88 mg, 68%) as a slightly greenish amorphous solid. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) $\delta = 7.05$ (d, $J = 8.3$ Hz, 2H), 6.96 (d, $J = 8.8$ Hz, 4H), 6.74 (d, $J = 8.1$ Hz, 2H), 6.55 (d, $J = 8.5$ Hz, 4H), 3.91 (br s, 2H), 3.57 (br s, 2H), 3.48 (br s, 2H), 2.95 (br s, 2H), 2.84 (s, 12H), 1.97 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS) $\delta = 158.4$, 150.0, 134.0, 130.2, 130.0, 129.4, 121.8, 114.7, 112.4, 69.9, 69.0, 67.4, 55.6, 48.1, 40.6, 25.0; MS CI $[MH]^+$ calcd 538, found 538.

Scheme 1. Self-Assembly and Disassembly of the UV-Responsive Polymeric Superamphiphile



Scheme 2. Synthetic Route to MG Molecule 2



1 **2**

Instruments. ^1H NMR spectra were recorded on a JEOL JNM-ECA600 spectrometer. UV/vis and fluorescence spectra were obtained on Hitachi U-3010 and Hitachi F-7000 spectrophotometers, respectively. UV light was provided by a high-pressure mercury lamp with an optical fiber and intensity of 900 mW/cm^2. Transmission electron microscopy (TEM) was performed on a JEMO 2010 electron microscope at an acceleration voltage of 110 kV. The samples for TEM observation were prepared by dropping the aqueous solution on the carbon-coated copper grid and staining with 0.2% phosphotungstic acid hydrate solution. Dynamic light scattering (DLS) was measured by a Nano ZS90 instrument, Malvern Instruments Ltd.

Preparation of Polymeric Superamphiphile. First the MG derivative was dissolved in water and neutralized with 1 equiv of sodium hydroxide at a concentration of 5×10^{-4} mol/L. PEG-*b*-PLKC was dissolved in pure water at a concentration of 4×10^{-6} mol/L, in which the concentration of the ammonium cation is 8×10^{-4} mol/L. Then 1.6 mL of the MG solution (the total amount of negative charge was 8×10^{-7} mol) was slowly added into 1 mL of the PEG-*b*-PLKC solution (the total amount of positive charge was 8×10^{-7} mol) under stirring, and the mixture was diluted with 2.4 mL of water for further experiments. The charge ratio of anionic MG and cationic PEG-*b*-PLKC in the polymeric superamphiphile (MG—PEG-*b*-PLKC for short) was 1:1. pH of the mixed solution is about 7, and the two aromatic tertiary amine groups are only slightly protonated, which should have little effect on the electrostatic interactions between the MG molecule and PEG-*b*-PLKC.

Fluorescence Measurements. Twenty microliters of a 5×10^{-4} mol/L Nile red solution in acetone was added to 1 mL of the polymeric superamphiphile solution described above or ro the polymeric superamphiphile solution irradiated with UV light for a certain time: 30, 60, 100, 300, or 900 s. Then the fluorescence spectra of the mixtures were recorded with excitation at 500 nm. The polarity of the solution can be estimated by the red shift and the quenching of fluorescence emission of Nile red.

■ RESULTS AND DISCUSSION

Photo-ionization of MG. To fabricate the UV-responsive polymeric superamphiphile, we first designed and synthesized the compound MG bearing a malachite green group, a well-known UV-sensitive chromophore. The chemical structure of MG is shown in Scheme 2. It is well-known that, upon UV irradiation, the malachite green group can exclude a CN$^-$,

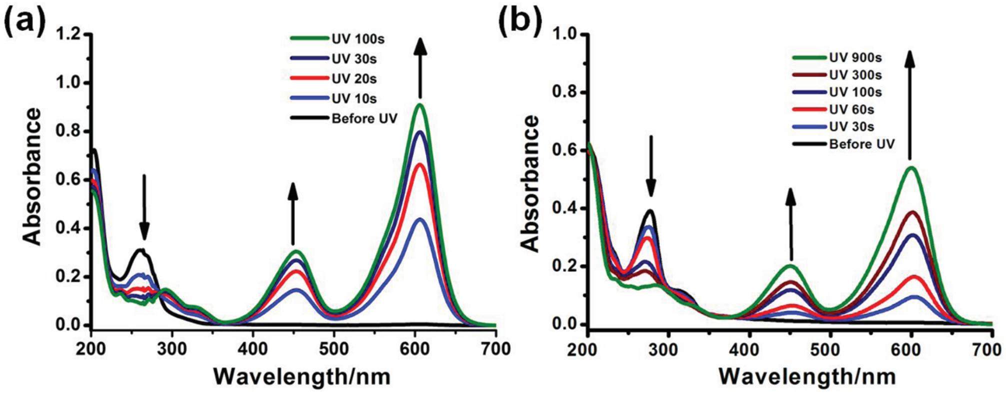


Figure 1. Photo-ionization of MG (a) without and (b) with PEG-*b*-PLKC. The concentration of MG in both solutions is 1.6×10^{-5} mol/L.

changing from a neutral hydrophobic moiety to a cationic hydrophilic moiety. Photo-ionization of the MG molecule was monitored by UV/vis spectrometry, as shown in Figure 1a. After UV irradiation, the colorless aqueous solution turns green and the absorbance at 606 and 453 nm increases quickly, while the absorbance at 259 nm drops dramatically. All these results show that the malachite green group undergoes an ionization process; that is, a CN^- is excluded from the molecule and a cationic state is formed.[10e] The photo-ionization process is considered as a first-order reaction, according to the formula $\ln[(A_0 - A_{eq})/(A_t - A_{eq})] = kt$, where the rate constant k is calculated as $0.078\ s^{-1}$. We wondered whether the photo-ionization could happen in the polymeric superamphiphile. UV/vis results for the polymeric superamphiphile are shown in Figure 1b. As can be seen, the malachite green group underwent the same photo-ionization process, but it needed a much longer time to reach photo-equilibrium. By the same formula mentioned above, the rate constant of the ionization of MG in the polymeric superamphiphile is calculated as $0.004\ s^{-1}$, which is much smaller than that of MG itself. This is reasonable because, in the polymeric superamphiphile, the interaction between the block copolymer and MG restricts the free movement of MG, and the block copolymer may absorb some UV irradiation, leaving less energy for the photo-ionization of MG.

Interaction between MG and PEG-*b*-PLKC. The interaction between MG and PEG-*b*-PLKC in aqueous environment was further demonstrated by NMR. As shown in Figure 2A, the protons H^a, H^b, H^c, and H^d on the aromatic rings of MG give very clear and sharp peaks between 6.9 and 7.2 ppm. After UV irradiation, the peaks of H^c and H^d move to lower field while the resonances of H^a and H^b are approximately the same. For the mixture of MG and PEG-*b*-PLKC, the protons on the aromatic rings of MG were all screened (Figure 2C), but they appeared after UV irradiation (Figure 2D). This is probably due to incorporation of MG into the superamphiphile and aggregation of the formed superamphiphile. The full incorporation resulted in the absence of MG proton signals. The results also indicate that the electrostatic interaction between MG and PEG-*b*-PLKC is able to induce formation of the polymeric superamphiphile and that the superamphiphile is disassembled after UV irradiation.

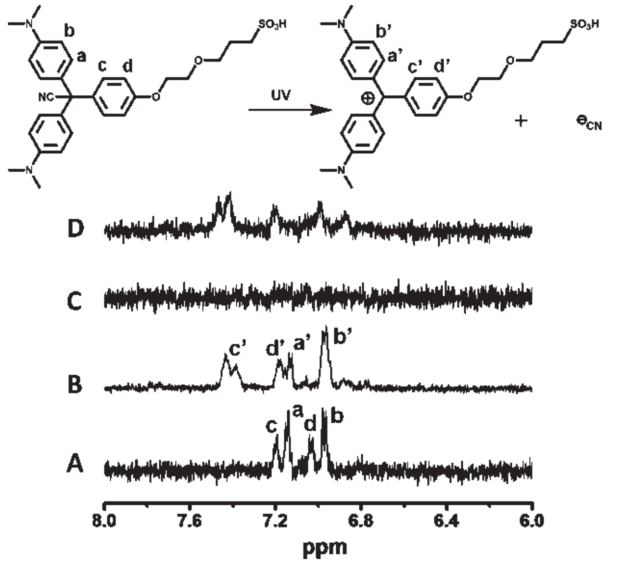


Figure 2. ^1H NMR of MG (A) before UV and (B) after UV for 600 s, and ^1H NMR of MG−PEG-*b*-PLKC (C) before UV and (D) after UV for 600 s. The concentration of MG is 1.6×10^{-4} mol/L in all solutions. The charge ratio of MG to PEG-*b*-PLKC is 1:1.

Self-Assembly of Polymeric Superamphiphile. We were curious about the self-assembled structure of the MG−PEG-*b*-PLKC superamphiphile. The critical micelle concentration (cmc) of MG is about 2×10^{-4} M, determined by measuring the conductivity as a function of increasing MG concentration. To avoid its own aggregation, the concentration of MG in the polymeric superamphiphiles is kept below its cmc. TEM is employed to observe the aggregated structure. As shown in Figure 3a,b, the polymeric superamphiphile self-assembles to form sheetlike aggregates in aqueous solution. Moreover, the sheetlike structure shows little change when the charge ratio of anion and cation is altered. Interestingly, upon UV irradiation, the sheetlike structure disappears, as shown in Figure 3c. The self-assembled sheetlike structure of the polymeric superamphiphile may be a result of $\pi-\pi$ interactions between the aromatic rings on the MG molecules. Upon UV irradiation, the MG molecules undergo an ionization process, switching from the anionic to the zwitterionic state, which strongly increases the solubility of the molecule and breaks the $\pi-\pi$ interaction between the aromatic rings due to charge repulsion, thus resulting in disassembly of the polymeric superamphiphile. It should

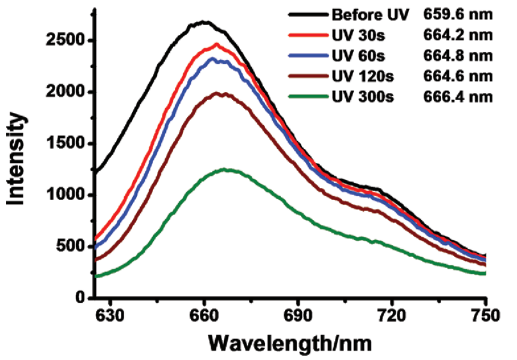


Figure 4. Fluorescence spectra of Nile red in 1:1 MG−PEG-*b*-PLKC solution with different UV irradiation times.

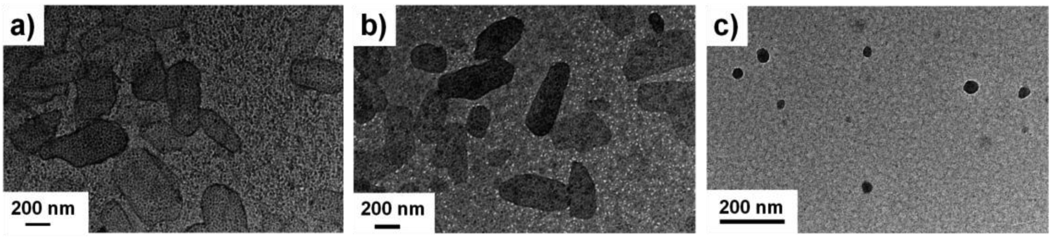


Figure 3. TEM images of MG−PEG-*b*-PLKC at charge ratios of (a) 1:2, (b) 1:1, and (c) 1:1 after UV for 300 s.

be noted that PEG-*b*-PLKC is doubly hydrophilic and cannot self-aggregate in the given concentration, as indicated by the DLS results that the count rate of the PEG-*b*-PLKC solution is approximately that of pure water.

Although DLS is a powerful technique to monitor the change of self-assembled structures in solution, the ionized MG has a strong absorption at 633 nm, which is a commonly used laser wavelength in DLS, making DLS not appropriate for monitoring the structure change of the polymeric superamphiphile during UV irradiation. Thus fluorescence spectroscopy was selected to monitor the structural change of the polymeric superamphiphile upon UV irradiation. Nile red was chosen as the probe. Normally, the emission of Nile red is red-shifted and quenched when the environment becomes more polar. From the results shown in Figure 4, it can be seen that the fluorescence emission of Nile red shifts to the red by about 7 nm after 300 s of UV irradiation and the intensity drops with increasing irradiation time. These results clearly show that the polarity of the solution increased after UV irradiation. In aqueous solution, the hydrophobic Nile red is usually incorporated in the hydrophobic part of the aggregates. Thus the results indicate an environment with higher polarity has been obtained after UV irradiation, which confirms the UV-induced disassembly of the MG−PEG-*b*-PLKC superamphiphile aggregates.

CONCLUSION

In summary, we have fabricated a UV-sensitive polymeric superamphiphile consisting of an anionic malachite green derivative and a cationic block copolymer on the basis of electrostatic interaction. The polymeric superamphiphile self-assembles into sheetlike aggregates in aqueous solution and disassembles under UV irradiation due to the increased solubility of MG. It is anticipated that a similar concept can be extended to fabricate stimuli-responsive polymeric superamphiphiles for controlled self-assembly and disassembly.

AUTHOR INFORMATION

Corresponding Author

*E-mail xi@mail.tsinghua.edu.cn.

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