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Poly(*p*-phenylene ethynylene)s with Facially Amphiphilic Pendant Groups: Solvatochromism and Supramolecular Assemblies

Yan Li,[a] Guangtao Li,*[a] Xinyan Wang,[b] Changxu Lin,[a] Yihe Zhang,[b] and Yong Ju*[a]

Abstract: Novel functionalized poly(*p*-phenylene ethynylene)s (PPEs) bearing facially amphiphilic cholic and deoxycholic acid units are synthesized by a Pd-catalyzed Sonogashira cross-coupling reaction. Some interesting properties, particularly their optical and self-assembly characteristics, are unraveled. The PPEs that carry bile acid substituents exhibit remarkable solvatochromism in a wide range of solvent systems, and judicious choice of the solvents can adjust the size and morphology of the formed nanoscale supramolecular aggregates. The incorporation of these naturally occurring building blocks can also impart biocompatibility to the conjugated system and stimulate the growth of living cells.

Keywords: amphiphiles · polymers · self-assembly · solvatochromism · supramolecular chemistry

Introduction

The construction of supramolecular architectures by the spontaneous self-assembly of conjugated polymers is under enthusiastic investigation owing to a wide academic interest and their important technological applications.[1] To tune the optoelectronic properties of the conductive polymer-based devices, the assembly of the polymer chains needs to be controlled. Amphiphilic block copolymers can generate various morphologies and their assembling mechanisms have been well studied.[2] However, their syntheses often requires time-consuming steps with nontrivial effort, especially for π-conjugated systems.[3] To minimize the tedious synthetic work in designing new self-assembling macromolecules, one can imitate and modify natural designs. Consequently, integration of biologically important molecules to a π-conjugated backbone seems to be a promising method to obtain supramolecular architectures that are capable of converting biomolecular structural information into physicochemical signals.[4]

Bile acids are a class of naturally occurring compounds with a facially amphiphilic steroid nucleus, and include the biologically important detergent-like substances cholic acid and deoxycholic acid.[5] The synthesis and structure elucidation of bile acid derivatives have been intensely studied from a pharmaceutical point of view.[6] Besides their biological importance, due to their unique facially amphiphilic character, bile acids have recently been presented as a versatile platform for the construction of environmentally responsive amphiphiles and functional supramolecular systems.[7] Regen et al. have described cholic acid based "molecular umbrellas" that can change their conformation as a function of solvent polarity.[8] Maitra et al. reported bile acid based chiral dendrons, which can act as both intramolecular normal and inverse micelles.[9] Recently, by taking advantage of the facial amphiphilicity and natural curvature, Zhao et al. described a type of cholate oligomer that could fold into a helical structure with a nanometer-sized hydrophilic cavity.[10]

In the present work, the synthesis of two functionalized poly(*p*-phenylene ethynylene)s (PPEs) bearing cholic and deoxycholic acid units, respectively (polymers **P1** and **P2** in Scheme 1), was demonstrated. These polymers were designed to preserve some properties of bile acids, such as facial amphiphilicity, capacity for self-assembling, biocompatibility, and the high chemical stability of the steroid nucleus, and also impart new optoelectronic properties through

[a] Y. Li, Prof. Dr. G. Li, C. Lin, Prof. Dr. Y. Ju
Department of Chemistry, Key Lab of Organic Optoelectronics & Molecular Engineering and
Key Lab of Bioorganic Phosphorus Chemistry & Chemical Biology, Tsinghua University
Beijing 100084 (China)
Fax: (+86) 10-6279-2905
E-mail: lgt@mail.tsinghua.edu.cn
juyong@mail.tsinghua.edu.cn

[b] X. Wang, Prof. Dr. Y. Zhang
School of Materials Science and Technology
China University of Geosciences
Beijing 100083 (China)

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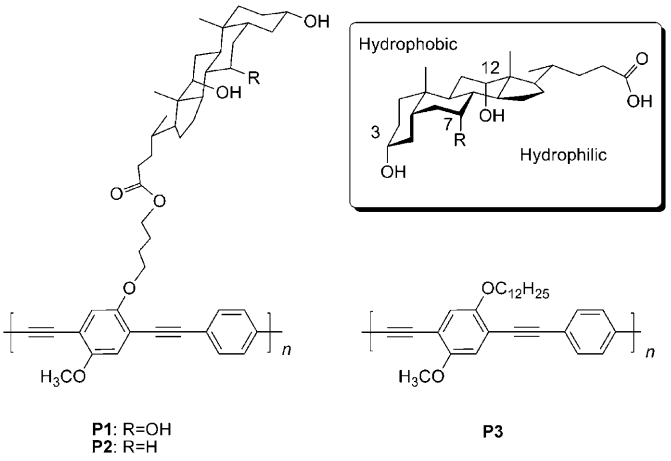
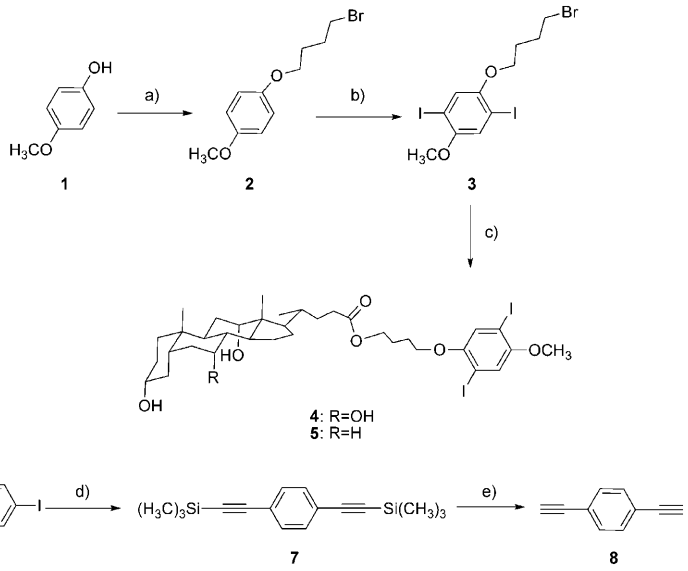


Scheme 1. Chemical structure of PPEs decorated with cholic (**P1**) and deoxycholic acid units (**P2**) as well as the model compound (**P3**). Inset: the stereochemical structure of bile acid.



Scheme 2. Synthesis of the corresponding monomers: a) $Br(CH_2)_4Br$, KOH, CH_3CN, RT; b) $AcOH/H_2SO_4/H_2O$ 30:1:2, KIO_3, I_2, 60 °C; c) sodium cholate, NaI, DMF, 65 °C; d) TMS, $[PdCl_2(PPh_3)_2]$, CuI, Et_3N, DMF, 60 °C; e) THF, CH_3OH, K_2CO_3.

the large π-conjugated system. It is worth mentioning that the first synthesis of bile acid derived polymers was described in 1988,[11] followed by a lot of contributions from Zhu's group,[12] due to the important biological applications. So far, however, most of the bile acid derived polymers synthesized rely on radical polymerization of the methacrylate group or direct condensation between carbonyl and hydroxyl groups. Much less is known about bile acid decorated conjugated polymers, and the incorporation of the bile acid moiety into conjugated systems to mediate the organization of polymer chains has never been reported.[13]

Results and Discussion

Synthesis: Scheme 2 displays the detailed synthetic routines. The cholic acid substituted monomers **4** were synthesized in three steps. The starting material was 4-methoxyphenol, which was etherified with 1,4-dibromobutane to obtain 1-(4-bromobutoxy)-4-methoxybenzene (75%). This intermediate was treated with iodine in the presence of an oxidant, which resulted in 1-(4-bromobutoxy)-2,5-diiodo-4-methoxybenzene (80%). Subsequent esterification with sodium cholate gave the desired monomer (86%). The polymers **P1** and **P2** were then obtained in relatively high yield (69 and 73%, respectively) by Sonogashira cross-coupling between their corresponding diiodide monomers (**4** and **5**) and 1,4-diethynylbenzene. This strategy is quite straightforward and simple, which eliminates the need for protection and deprotection of terminal hydroxyl groups on the steroid nucleus. For control experiments, a similar polymer **P3** without a bile acid pendant group was also synthesized and used as the model compound.

Optical and self-assembly properties: The newly synthesized polymers (**P1** and **P2**) are sparingly soluble in toluene and water, but dissolve well in aprotic polar solvents, such as THF and DMF, to form clear blue/green fluorescent solutions. Figure 1 indicates that the UV/Vis and emission spectra of **P1** in the solid state were significantly broadened and red-shifted relative to its solution spectra, due to aggregation and excimer formation (also see Table S1 in the Supporting Information). However, the difference in the optical spectra of **P1** in THF solution and spin-cast thin films is relatively small compared to those for the model compound **P3**, which suggests that the large, rigid bile acid skeletons can ensconce the polymer chain to some extent, and act as an insulator against intermolecular chain interaction.

The solvatochromism of the conjugated polymer system is due to the transition between a twisted conformation to planar or nearly planar assemblies in solvents with different polarity, which is well demonstrated through the introduction of side chains, especially alkyl or polyethylene oxide substituents, into the conjugated backbone.[14] As described in the Introduction, cholic acid is an interesting compound that is uniquely suitable for solvophobically driven conformational changes.[15] The integration of such an environmentally sensitive building block into the conjugated π system was expected to endow the prepared polymers with remarkable solvatochromism. Figure 2a shows the UV/Vis absorption spectra of **P1** in dioxane/water mixtures. An absorption band with a maximum at $\lambda = 408$ nm was observed for **P1** in pure 1,4-dioxane, which is a good solvent for both hydrophilic and hydrophobic moieties. With the progressive addition of water, the absorption band becomes broader and the maximum of the UV/Vis absorption gradually shifts from 408 to 448 nm, accompanied by an 80% loss of fluorescence (Figure 2b). The facially amphiphilic character of the bile acid unit prompted us to examine the solvatochromic behavior in nonpolar media. Indeed, with the gradual addition of

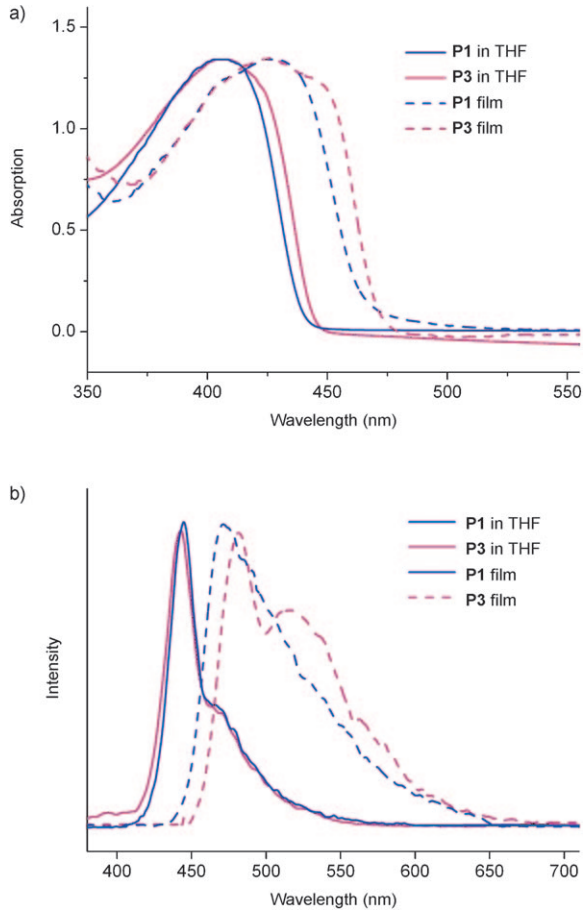


Figure 1. a) Normalized UV/Vis absorption spectra of **P1** and **P3**. b) Normalized emission spectra of **P1** and **P3**.

cyclohexane to dioxane, a dramatic red shift of the UV/Vis spectra and a modest quenching of fluorescence were also observed for **P1** (Figure 2c and d). The maximum absorption at $\lambda = 408$ nm continuously red-shifts to $\lambda = 441$ nm, which is also typical of a PPE chain with a high conformational order. The profile of this UV/Vis spectrum is sharper and quite different from the absorption in the polar medium, which suggests that different modes of intermolecular association are involved in the aggregation.

The optical transition described above can be manipulated continuously and reversibly by varying the ratio of the selective solvents in the polymer solution. The aggregation of cholate units induced by the presence of water or cyclohexane could lead to a more planar conformation of the PPE backbone, which should be the most probable reason for the observed solvatochromism.[16]

With the increase of water content, it is interesting to note that the transparent blue fluorescent solution of **P1** in dioxane changes to a yellowish green cloudy liquid, which exhibits scattering of daylight (Tyndall effect, characteristic of nontrue solutions; see Figure 3). The optoelectronic features of conductive polymers are strictly related to their aggregation states and strongly depend on the microstructural environment; therefore, the dramatic difference in UV/Vis absorption should be a reflection of different aggregate states of the polymers in solution. To test our hypothesis, a dynamic light scattering (DLS) experiment was performed. Figure 3 shows the effect of water content on the effective diameter (ED) of the resulting aggregates measured from solutions of **P1** and **P2** in water/dioxane mixtures. At a water content of less than 20%, the EDs for the two polymers are less than 200 nm. As the water content increases, both polymers show a rapid increase in the particle size as well as the polydispersity (Figure S1 in the Supporting Information).

We wondered how the presence of nonsolvents could affect the morphological transitions of bile acid derived PPEs. To address this question, the assembling of polymer **P1** in dioxane ($0.1\ mg\,mL^{-1}$) with increasing percentage of water was monitored by SEM. Such an approach was in line with the methodology that has been successfully set up by Eisenberg's group for self-directed assemblies of block polymers.[17] At a volume fraction of water of 20%, spherical particles with a diameter of 200 to 400 nm were observed (Figure 4a). A few of the particles formed open holes on their surfaces, which suggests that they had a hollow interior. TEM was used to confirm this possibility and substantiate whether or not these spherical particles are hollow in nature. Both capsulelike and solid structures were observed in the TEM images, thus indicating that the spherical aggregates in the SEM images were in fact a mixture of small vesicles and micelles (see Figure 4 and Figure S2 in the Supporting Information).

With the progressive addition of water, the aggregates grew bigger and the size distribution became broader. When the water content was increased to about 40%, much larger vesicles with diameters up to 1 μm and remarkably thick membrane walls turned out to be the dominant structure (Figure 4b). Interestingly, unlike many other reported vesicles that showed an immediate collapse on solid surfaces,[18] the SEM images revealed that in our case the formed PPE vesicles retained their shape upon drying, presumably due to the rigid steroid nucleus and the conjugated backbone. A similar self-assembly behavior can also be produced by the incremental addition of water to THF instead of dioxane (Figure 4c). However, when only a few drops of DMF or DMSO (a powerful hydrogen-bond breaker[19]) are present, the vesicle-like structure collapses and ill-defined precipitates form (Figure 4d), thus indicating that hydrogen bonds play an essential role in the formation of the observed nanostructures.

The self-assembly properties of **P1** in nonpolar media were also investigated. In this respect, cyclohexane was progressively added to a 1,4-dioxane solution of **P1**. Notably, well-defined, small, spherical solids were found in the SEM images on addition of small amounts of cyclohexane. The TEM image in Figure 5a reveals that the uniform spherical particles have a solid interior with a diameter of approximately 300 nm. The aggregates gradually changed to relatively large spherical particles with an increase in the cyclohexane content (Figure 5b). This result demonstrates that

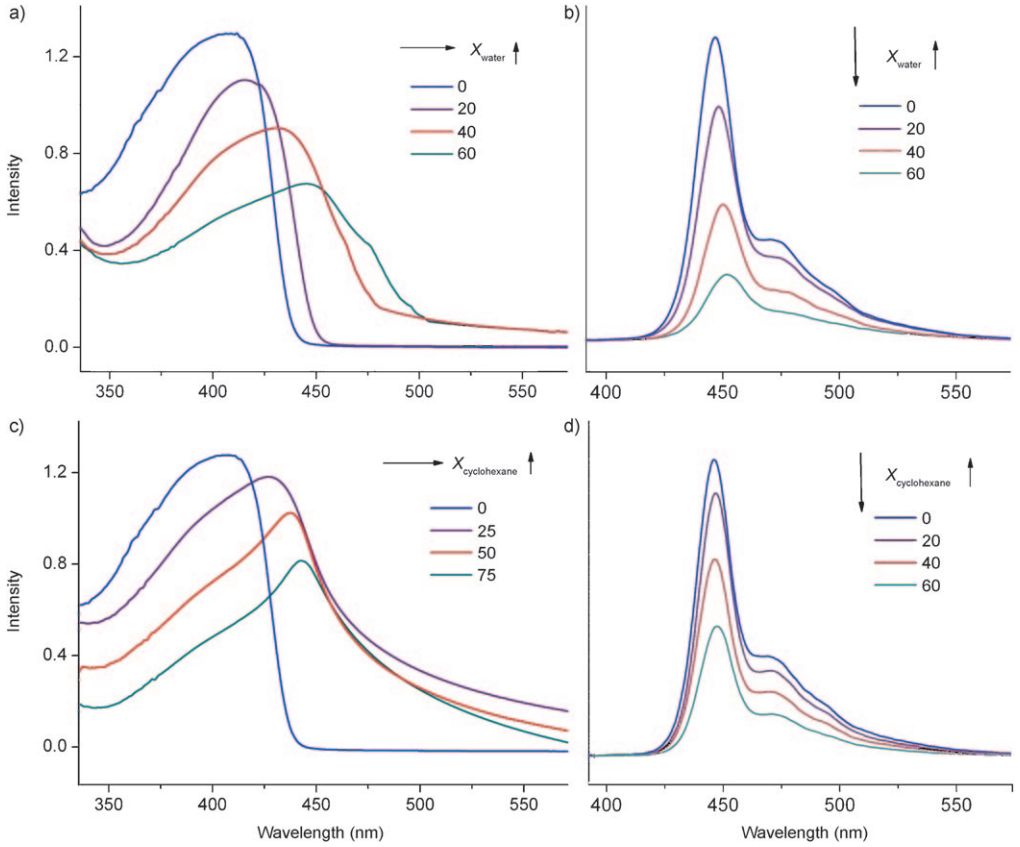


Figure 2. a) UV/Vis absorption and b) emission spectra of **P1** in dioxane at 20 °C as a function of added water; c) UV/Vis absorption and d) emission spectra of **P1** in dioxane at 20 °C as a function of added cyclohexane. Insets: the content of nonsolvent in %.

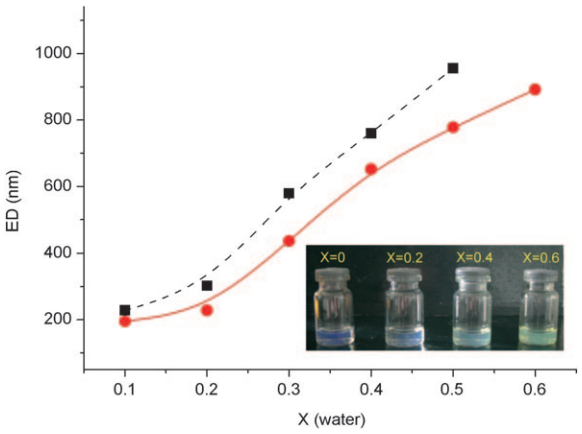


Figure 3. Effective diameter (ED) determined by dynamic light scattering (DLS) of **P1** and **P2** (0.1 mg mL^{-1}) in water/dioxane solution as a function of the volume fraction of water at 20 °C. Inset: color transition of **P1** in water/dioxane mixtures. See Figure S1 in the Supporting Information for the original DLS spectrum of **P1**. ●: **P1**; ■: **P2**.

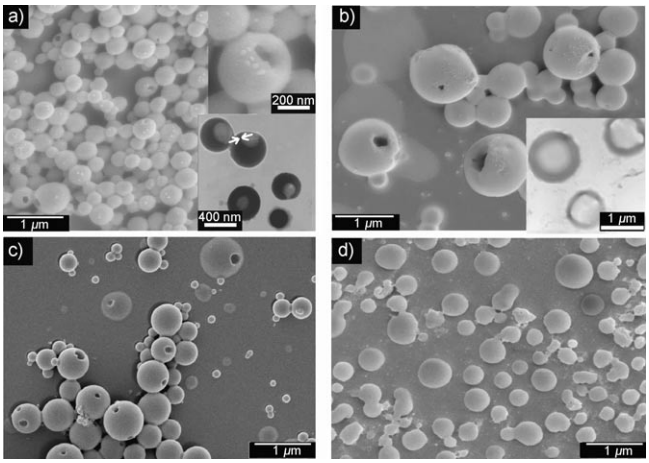


Figure 4. a,b) SEM and TEM (insets) images of the supramolecular aggregate formed from **P1** by using a water/dioxane system with a volume fraction of water of a) 25 and b) 50 %. Arrows in inset of (a): slightly tilted membrane site (see text). c) SEM image of the aggregate from **P1** in water/THF solution with a volume fraction of water of 40 %; d) as in (c), but with 50 μL dimethyl sulfoxide (DMSO) added.

the polymer **P1** exhibits quite different self-assembly behavior in polar and nonpolar media.

To clarify the role of the facially amphiphilic moiety in the solvatochromic behavior and in the formation of supramolecular aggregates, polymer **P2**, in which pendant groups with less facial amphiphilicity were attached, was also investigated. It was found that the deoxycholic acid decorated polymer (**P2**) exhibited similar solvatochromic behavior to

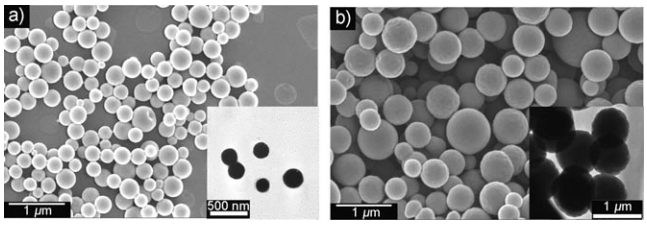


Figure 5. SEM and TEM (insets) images of the supramolecular aggregate formed from **P1** by using a cyclohexane/dioxane solvent mixture with a volume fraction of cyclohexane of a) 30 and b) 60%.

that of the cholic acid decorated polymer (**P1**) in the water/dioxane system (Figure 6a). Large vesicles were also found in the freshly prepared water/dioxane solution, though the uniformity and stability of the formed vesicles have clearly deteriorated compared to those of **P1** (Figure 7a). Although most of the **P1**-derived vesicles retained their shape without obvious changes in morphology during storage, **P2**-derived vesicles deformed seriously and many of them turned into irregular aggregates after two days at room temperature (Figure 7c and d). Different from the water/dioxane system, only modest solvatochromism was observed for **P2** in non-

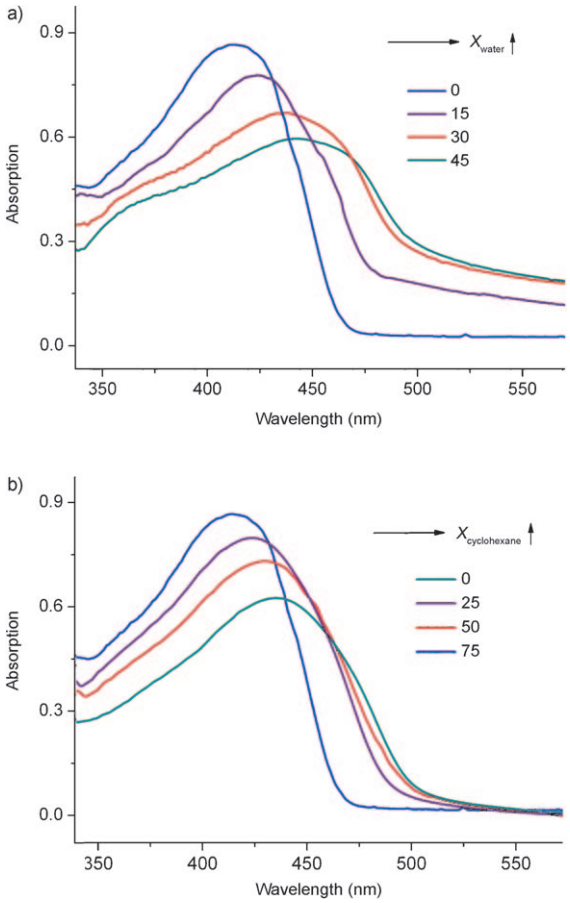


Figure 6. UV/Vis absorption spectrum of **P2** in dioxane at 20°C as a function of added a) water and b) cyclohexane. Insets: the content of nonsolvent in %.

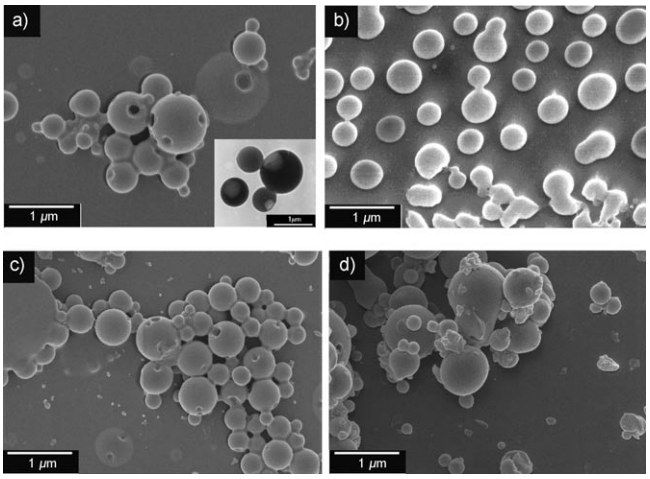


Figure 7. a,b) SEM and TEM (inset) images of the supramolecular aggregate formed from **P2** by using a) a water/dioxane mixture with a volume fraction of water of 40% and b) a cyclohexane/dioxane mixture with a volume fraction of cyclohexane of 70%. c,d) SEM images of the aggregates formed from c) **P1** and d) **P2** which was stored in a water/dioxane mixture ($X_{water}=40\%$) for 48 h at room temperature.

polar media (Figure 6b). In contrast to the solid spherical particles observed for **P1**, there is only a round, disklike residue upon natural evaporation of a cyclohexane/dioxane solution of polymer **P2** (Figure 7d). As a control experiment, polymer **P3** without facially amphiphilic side chains shows a negligible solvatochromism (Figure S3 in the Supporting Information) and does not afford any regular self-assembled aggregate under the same conditions (Figure S4). The results described above unambiguously indicate that the attached facially amphiphilic cholate groups can mediate the organization of PPE chains and donate remarkable solvatochromism in cooperation with a conjugated polymer system.

Mechanism of self-assembly: The self-assembly of bile acid conjugates has recently been used to prepare a number of distinct nanostructured materials, such as micelles, vesicles, giant needles, and nanotubes.[20] The mechanism of their formation is quite complex and often involves complicated "secondary assemblies". Figure 8a summarizes the aggregation behavior of cholic acid decorated PPE, which shows different buildups of supramolecular assemblies dependent upon the conditions used. This novel cholic acid functionalized PPE has a unique structure that is distinguishable from that of the classical amphiphilic block polymers: every pendant group possesses two distinguishable faces and as such is capable of showing aggregation behavior in both polar and nonpolar media through different modes of intermolecular association.

In polar media, the self-assembly should be a combination of three driving forces. One is the hydrophobic interaction that is attributed to the polymer backbone and the hydrophobic face of cholic acid and the spacer between the above two moieties. Another is the π–π stacking interaction provided by the large π-conjugated system. Considering the

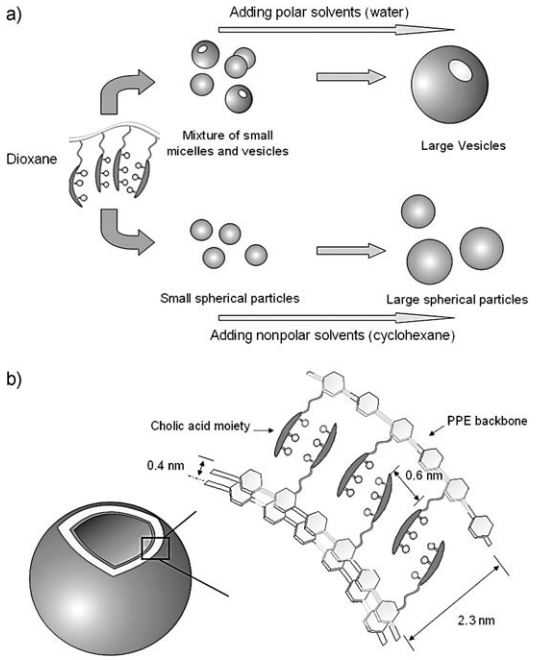


Figure 8. Schematic illustration of a) the morphology transition of cholic acid decorated PPE in solvents with different polarity and b) the proposed molecular packing model of cholic acid decorated PPE in the membrane of the formed vesicular structure.

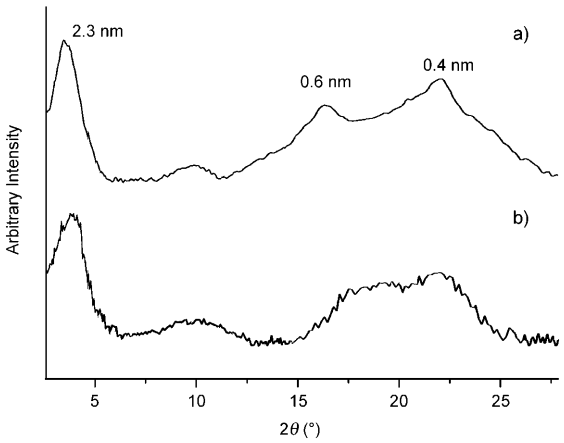


Figure 9. XRD patterns of the vesicular structures formed from a) **P1** and b) **P2**.

fact that DMSO interferes with the self-assembly process, hydrogen bonding probably also plays a key role in the formation of vesicles. The occurrence of hydrogen bonds is attributed to the hydroxyl groups on the adjacent cholic acid units. Very likely, one or two water molecules might also be present and act as bridging groups between cholate hydroxyl groups, as is seen in the crystal structure of cholic acid.[21]

In the case of nonpolar media, hydrogen bonding and π–π stacking should be strongly involved in the self-assembly process. Cyclohexane is a good solvent for the hydrophobic face of cholic acid, but a nonsolvent for the hydroxyl groups on the steroid nucleus. Thus, the hydrophilic face tends to aggregate through intermolecular hydrogen bonding. Probably due to the absence of hydrophobic interactions, the packing among the polymer chains was less compact and organized compared to that in the polar media, which might be responsible for the distinctive profiles of UV/Vis absorption in solvents with different polarity.

X-ray diffraction (XRD) experiments on the supramolecular aggregate formed from **P1** in polar medium were used to probe the molecular packing in the membrane of the vesicular structure. The XRD patterns showed Bragg peaks at $2\theta = 3.9$, 16.3, and 22.4°, corresponding to the d spacing at 2.3, 0.6, and 0.4 nm, respectively (Figure 9). Theoretically, the space between the π-conjugated backbone and the end of the steroid nucleus (C3 atom) is about 2.0 nm, based on the assumption that the alkyl spacer takes the fully extended conformation. The thickness of the cholate unit is about 0.5 nm[20c] and the distance between π-stackings of PPE is estimated as about 0.4 nm.[22] It has been generally recognized that bile acid derivatives tend to assemble in a head-to-tail fashion with two distinguishable faces of the cholates tilted up and down alternately,[20] whereas PPE derivatives with long alkyl or alkoxy groups were expected to form a lamellar or doubly lamellar morphology in which the structure of the polymer is dominated by side-chain packing.[23] Based on the data and results described above, we proposed that the molecular packing in the membrane of the formed vesicular structure has a multilayer lamellar structure through a combination of hydrogen bonding, hydrophobic interaction, and π–π stacking, in which the conjugated molecule is arranged in a highly organized pattern and the bile acid units are in an antiparallel interlocked configuration (Figure 8b). Measurement of the membrane-wall thickness at the slightly tilted membrane site (marked by the arrows in Figure 4a) gave an edge width of about 20–25 nm for the relatively small vesicles. These distances across the membrane wall fit approximately with 9–11 layers of the proposed structural units. The alkyl tail might be a little coiled because the longitudinal length is a bit longer than the distance calculated from the Bragg equation. The XRD result also suggests that the molecular packing of **P2** in the membrane was less organized than that of **P1** (Figure 9b), which accounts for the poor stability of the vesicle formed. The poor stability is consistent with the fact that the hydroxyl group at position 7 plays an important role in building the amphiphilic structure and forming the stable interdigitated structure.[24]

Different from the vesicular structure, **P1** affords spherical solid particles in nonpolar media that reveal a very broad diffraction peak between 15 and 25° (2θ) in the XRD spectrum (not shown), thus indicating the amorphous nature of these aggregates. However, it is still not clear how to explain the formation of these well-defined solid particles with diameters of a few hundred nanometers, and further investigation is required.

The origin of large vesicles and micelles was expected to be the fusing of small aggregates. The driving force behind the fusion process might be the release of strain in the initially formed small assemblies, which have high curvature

and many surface defects, and as such lead to a more thermodynamically stable state.[25] Increasing the content of poor solvents, such as cyclohexane and water, leads to the aggregation of cholate moieties and facilitates the fusion step. This process is accompanied by the stacking and planarization of π-delocalized backbones, which results in quenching of the fluorescence and a concomitant red shift in the UV/Vis spectra.

Perfectly regular stacking of identical π-conjugated systems would lead to a ribbonlike structure;[26] the formation of spherical aggregates requires bending of the semirigid PPE backbone. However, it is still unclear where the curvature comes from in our case. The report by Bunz et al. shows that bending of the conjugated backbone can be induced by the large side-chain substituent according to molecular mechanics calculations.[27] In this respect, we speculated that the curvature of **P1** and **P2** in the formed aggregates was contributed to by the large, rigid steroid moiety and/or by the inhomogeneity of the polymer chain length, which is related to the polydispersity.

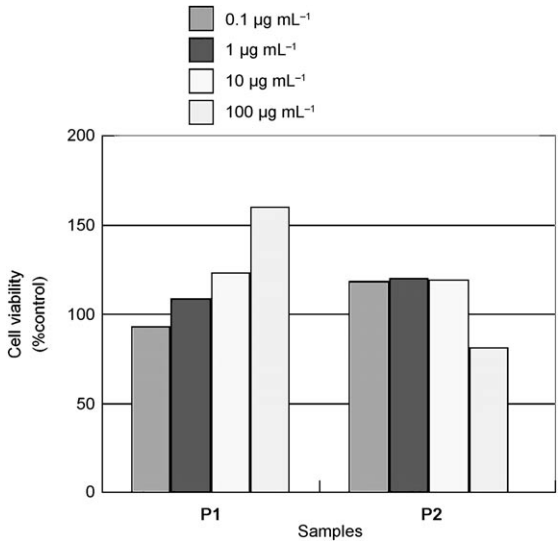


Figure 10. Influence of **P1** and **P2** on the growth of HeLa cells at different concentrations.

Bioactivity test: Compounds derived from bile acids are expected to be safe and nontoxic when used in the biomedical and pharmaceutical fields.[28] Decorating the synthetic polymers with these naturally occurring pendant groups is expected to impart biocompatibility to the conjugated polymers. To check whether our bile acid-containing PPEs are biocompatible, we studied the cytotoxicity of **P1** and **P2** to living HeLa cells. DMSO solutions of **P1** and **P2** with a concentration of 1 mg mL^{-1} were prepared and further diluted 1000 times with the culture medium. Different amounts of **P1** and **P2** were added to 24-well plates a few hours after the cells were seeded. A well without the addition of polymer solution served as a control. All data shown are means of values in three independent experiments, and the mean values of each group were compared with the blank control experiment (see Figure 10). At a concentration of 0.1 μg mL^{-1}, the cell population of **P1** is comparable to that of the blank experiment. Interestingly, with the increase of the polymer concentration the cell population became even higher, which proves that this polymer is cytocompatible. On the contrary, **P2** shows slight cytotoxicity at high concentration. The better biocompatibility of **P1** is probably derived from its remarkable facially amphiphilic structure that enables the polymer to interact more favorably with the biological environment. We have attempted to study the cytotoxic effect of the model compound **P3**, but were hindered by its poor solubility in the aqueous media.

Conclusion

We have demonstrated that the incorporation of facially amphiphilic bile acid moieties is an effective approach to guide the self-assembly of PPE chains. Due to their unique facially amphiphilic character, bile acid decorated PPEs exhibit remarkable solvatochromism not only in polar solvents but also in nonpolar systems. Of particular significance is the fact that judicious choice of the solvents affords the synthesis of nanoscale assemblies with adjustable size and morphology. Besides being the first example of bile acid group mediated self-assembly of PPEs, the current work offers a new means to control the association and optoelectronic properties of conjugated backbones, which is anticipated to be extendable to other conjugated polymer systems. Moreover, the combination of bile acids and conjugated polymers leads to biocompatible functional materials, which could find various applications in photosensitive therapy, controlled-release systems, or as a scaffold material in tissue engineering.

Experimental Section

Cholic acid, deoxycholic acid, trimethylsilylacetylene (TMS), and 1-bromododecane were purchased from Sigma Company. $[Pd(PPh_3)_4]$ was obtained from Pingyang Chemical Company and washed with cold ethanol prior to use to remove the oxidized impurity. Other reagents and solvents were received from Beijing Chemical Company and used without further purification unless otherwise stated. 1,4-Diethynylbenzene[29] and 4-dodecyloxy-2,5-diiodo-1-methoxybenzene[30] were prepared and characterized according to previously published procedures. Full experimental details are included in the Supporting Information.

1-(4-Bromobutoxy)-4-methoxybenzene (2): A mixture of 4-methoxyphenol (3.723 g, 30 mmol), potassium carbonate (6 g), and 1,4-dibromohexane (10.795 g, 50 mmol) in acetone (70 mL) was heated at reflux for 20 h. The precipitated potassium bromide was isolated by filtration and acetone was removed with a rotary evaporator. The final product **2** was recrystallized from methanol as a white solid (5.8 g, 75%). M.p.: 46–47 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.88–1.98 (m, 2H; CH_2), 2.02–2.12 (m, 2H; CH_2), 3.48 (t, 2H; CH_2Br), 3.76 (s, 3H; OCH_3), 3.94 (t, 2H; OCH_2), 6.82 ppm (s, 4H; Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.98, 28.65, 33.68, 55.83, 68.35, 114.76, 115.56, 153.25, 153.91 ppm.

1-(4-Bromobutoxy)-2,5-diiodo-4-methoxybenzene (3): Water (2 mL), acetic acid (30 mL), concentrated sulfuric acid (1 mL), **2** (1.94 g, 7.5 mmol), potassium iodate (856 mg, 4 mmol), and iodine (2.0 g,

3.9 mmol) were stirred at 60 °C for 4 h. After cooling to room temperature, the excess iodine was destroyed with an aqueous sodium sulfite solution (10 %), and the reaction mixture was poured into ice water (300 mL). The aqueous phase was extracted with diethyl ether (3× 30 mL), and the solvent of the combined organic layers was evaporated. Purification of the residue by means of column chromatography (silica gel, hexane/EtOAc 50:1) resulted in a colorless solid (3.1 g, 6 mmol, 80 %). M.p: 50–51 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.90–2.00 (m, 2H; CH_2), 2.06–2.17 (m, 2H; CH_2), 3.52 (t, 2H; CH_2Br), 3.81 (s, 3H; OCH_3), 3.96 (t, 2H; OCH_2), 7.17 ppm (s, 2H; Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 27.88, 29.61, 33.74, 57.34, 63.35, 85.65, 86.48, 121.54, 123.00, 152.70, 153.51 ppm.

1-[4-(3α,7α,12α-Trihydroxy-5β-cholan)butoxy]-2,5-diiodo-4-methoxybenzene (4): Sodium cholate (1 mmol, 0.449 mmol) was added to a solution of **3** (511 mg, 1 mmol) and NaI (0.75 mmol, 100 mg) in DMF (20 mL), and the reaction mixture was stirred at 65 °C for 4 h. The mixture was then cooled, poured into water (100 mL), and extracted with EtOAc (30 mL) twice. The organic layer was washed with H_2O (30 mL) and aqueous $NaHCO_3$ solution (30 mL). The crude product obtained after removal of the solvent was purified by chromatography on silica gel with 4 % MeOH/CH_2Cl_2 as eluent to give **4** (0.50 g, 51 %) as a white solid. M.p: 96–97 °C; IR: $\tilde{\nu}$ = 3450, 2940, 2860, 1740, 1650, 1470 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.68 (s, 3H; 18-CH_3), 0.89 (s, 3H; 19-CH_3), 0.98 (d, 3H; 21-CH_3), 1.10–2.40 (m, 31H; aliphatic H), 3.43–3.49 (m, 1H; 3α-CH), 3.82–3.86 (m, 4H; OCH_3, 7α-CH), 3.93–4.02 (m, 3H; OCH_2, 12α-CH), 4.16 (t, 2H; -$COOCH_2$), 7.18 ppm (d, 2H; Ar-H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ = 12.64, 17.46, 22.60, 23.33, 25.58, 26.01, 28.33, 30.56, 31.03, 31.43, 34.71, 34.82, 27.60, 35.29, 35.35, 39.64, 39.74, 41.56, 41.88, 46.57, 47.18, 57.28, 64.00, 68.55, 69.75, 72.03, 73.11, 85.52, 86.43, 121.59, 123.04, 152.82, 153.50, 174.44 ppm; HRMS (ESI): *m*/*z*: calcd for $[C_{35}H_{52}I_2O_7+Na]^+$: 861.1700; found: 861.1688.

1-(4-(3α,12α-Dihydroxy-5β-deoxycholan)butoxy)-2,5-diiodo-4-methoxybenzene (5): This compound was synthesized by using the same procedure as described for **4**, with deoxycholic acid instead of cholic acid. M.p: 78–79 °C; IR: $\tilde{\nu}$ = 3450, 2930, 2860, 1730, 1660, 1490 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.67 (s, 3H; 18-CH_3), 0.91 (s, 3H; 19-CH_3), 0.98 (d, 3H; 21-CH_3), 1.10–1.95 (m, 31H; aliphatic H), 2.17–2.52 (m, 2H; 23-CH_2), 3.52–3.63 (m, 1H; 3α-CH), 3.82 (m, 3H; OCH_3), 3.97 (brs, 4H; OCH_2, 12α-CH), 4.16 (t, 2H; −$COOCH_2$), 7.18 ppm (d, 2H; Ar-H); ^{13}C NMR ($CDCl_3$, 300 MHz): δ = 12.87, 17.43, 23.26, 23.58, 25.75, 26.00, 26.21, 27.21, 27.56, 28.76, 30.59, 31.01, 33.76, 34.20, 35.17, 35.30, 36.12, 36.52, 42.17, 46.59, 47.42, 48.35, 57.28, 63.98, 69.75, 71.90, 73.23, 85.51, 86.42, 121.58, 123.04, 152.81, 153.50, 174.36; HRMS (ESI): *m*/*z*: calcd for $[C_{35}H_{52}I_2O_6+Na]^+$: 845.1751; found: 845.1745.

Cholic acid decorated PPE (P1): Compound **4** (822 mg, 0.8 mmol), 1,4-diethynylbenzene (101 mg, 0.8 mmol), [$Pd(PPh_3)_4$] (10 mg), and CuI (3 mg) were dissolved in a mixture of (iPr)$_2$NH (1.5 mL) and THF (3.5 mL). The solution was stirred under an N_2 atmosphere at 50 °C for 24 h. After cooling the reaction mixture to room temperature, the salts were filtered, the filtrate was poured into acetone (100 mL), and the precipitated solid was collected by filtration. The resulting solid was redissolved and precipitated into a large amount of methanol (200 mL). A bright-yellow polymer **P1** (0.394 g, 69 %) was obtained. The product was dried under vacuum for 24 h before characterization. The number-average molecular weight (M_n) was measured by gel-permeation chromatography (GPC; eluent: THF). Weight-average molecular weight M_w = 30422, M_n = 20927; polydispersity index (PDI) = 1.45; IR: $\tilde{\nu}$ = 3493, 2910, 2809, 1725, 1430 cm^{-1}; ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ = 0.71 (s, 3H; 18-CH_3), 0.85 (s, 3H; 19-CH_3), 0.99–2.20 (m, 36H), 3.39 (m, 1H; overlaps with the peak of the water signal, 3-CH), 3.82–3.91 (m, 4H; OCH_3, 7-CH), 4.05 (m, 3H; OCH_2, 12-CH), 4.36 (d, 2H; OCH_2), 6.97–7.06 (m, 2H; Ar-H), 7.52 ppm (brs, 4H; Ar-H); elemental analysis calcd (%) for $(C_{45}H_{56}O_7)_n$: C 76.24, H 7.96; found: C 76.15, H 8.81.

Deoxycholic acid decorated PPE (P2): This compound was synthesized by using the same procedure as that described for **P1**. Note that **P2** has much better solubility in $CHCl_3$ than **P1**. The M_n was measured by GPC (eluent: THF): M_w = 32901, M_n = 21138; PDI = 1.56; yield: 73 %; IR: $\tilde{\nu}$ = 3508, 2908, 2790, 1708, 1480 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.64–0.68 (s, 3H; 18-CH_3), 0.78–2.39 (m, 39H), 3.52–3.69 (brs, 1H; 3-CH), 3.90 (brs, 3H; OCH_3), 3.90–4.10 (m, 3H; OCH_2, 12-CH), 4.08–4.20 (d, 2H; OCH_2), 7.00–6.93 (m, 2H; Ar-H), 7.52 ppm (brs, 4H; Ar-H); elemental analysis calcd (%) for $(C_{45}H_{56}O_6)_n$: C 78.00, H 8.15; found: C 77.58, H 9.30.

Synthesis of the model polymer (P3): Compound **4** (544 mg, 1 mmol), 1,4-diethynylbenzene (126 mg, 1 mmol), [$Pd(PPh_3)_4$] (10 mg), and CuI (3 mg) were dissolved in a mixture of (iPr)$_2$NH (1.5 mL) and THF (3.5 mL). The solution was stirred under an N_2 atmosphere at 50 °C for 24 h. The reaction mixture was extracted with $CHCl_3$ (50 mL) and washed with 10 % HCl (50 mL), saturated aqueous $NaHCO_3$, and brine (2×50 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The remaining residue in $CHCl_3$ (5 mL) was poured into a large amount of methanol (150 mL) to precipitate the yellow solid **P3** (0.331 g, 80 %). M_n was measured by GPC (eluent: THF): M_n = 12750; PDI = 1.72; IR: $\tilde{\nu}$ = 2920, 2860, 1520, 1380, 1210, 831 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.89 (brs, 3H), 1.29 (brs, 16H), 1.50–1.60 (m, 2H), 1.80–1.95 (m, 2H), 3.89 (brs, 3H; OCH_3), 3.98–4.20 (m, 2H), 6.92–7.04 (m, 2H), 7.53 ppm (brs, 4H); elemental analysis calcd (%) for $(C_{29}H_{34}O_2)_n$: C 84.02, H 8.27; found: C 83.71, H 8.50.

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