SUPRAMOLECULAR CHEMISTRY: FROM MOLECULAR ARCHITECTURES TO FUNCTIONAL ASSEMBLIES

Huaping Xu and Xi Zhang

Department of Chemistry, Tsinghua University, Beijing 100084, China

Junqi Sun

State Key Lab for Supramolecular Structures and Materials, Jilin University, Changchun 130021, China

Shuxun Cui

Key Laboratory of Advanced Technologies of Materials, Southwest Jiaotong University, Chengdu, 610031, China

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Contents

Summary

Supramolecular Chemistry aims at developing highly complex chemical systems from components in interacting by noncovalent intermolecular forces. As initiated by J. M. Lehn, the field was and is the basis for most of the essential biochemical processes of life. It has grown over twenty years into a major domain of modern teaching, research and technology. It has fueled numerous developments at the interfaces with biology, physics, materials science and biomedicine, thus giving rise to the emergence and establishment of supramolecular science, today a broad multidisciplinary and interdisciplinary domain, providing a highly fertile ground for creative cooperation of scientists from very different backgrounds. First and foremost among the motivations for exploring supramolecular chemistry is the desire to synthesize new robust, functional, and technologically important materials by mimicking nature. In nature, organization on the nanometer scale is crucial for the remarkable properties and functional capabilities of biological systems. A second impetus is the desire to design, using functional small-molecule building blocks, new synthetic materials that feature even more useful ensemble properties emanating directly from nanoscale and microscale ordering. Lastly, the need for improved miniaturization and device performance in the microelectronics industry has inspired many investigations into supramolecular chemistry.

1. Introduction

For over 100 years, chemistry has focused primarily on understanding the behavior of molecules and their construction from constituent atoms. Our current level of understanding of molecules and chemical construction techniques has given us the confidence to tackle the construction of virtually any molecule, be it biological or designed, organic or inorganic, monomeric or macromolecular in origin. During the last

three decades, chemists have extended their investigations beyond atomic and molecular chemistry into the realm of supramolecular chemistry. Terms such as molecular self-assembly, hierarchical order, and nano-science are often associated with this area of research. Broadly speaking, supramolecular chemistry is the study of interactions between, rather than within, molecules—in other words, chemistry using molecules rather than atoms as building blocks. Whereas traditional chemistry deals with the construction of individual molecules (1–100 Å length scale) from atoms, supramolecular chemistry deals with the construction of organized molecular assemblies with much larger length scales (1–100 nm). In molecular chemistry, strong association forces such as covalent and ionic bonds are used to assemble atoms into discrete molecules and hold them together. In contrast, the forces used to organize and hold together supramolecular assemblies are weaker noncovalent interactions, such as hydrogen bonding, polar attractions, van der Waals forces, hydrophilic–hydrophobic interactions and charge transfer interaction.

Amphiphilicity is one of the molecular bases for supramolecular assemblies. By tuning the amphiphilicity of the building blocks, the controllable self-assembly and disassembly can be realized, leading to fabrication of new functional supramolecular assemblies and materials. Besides the supramolecular assembly in solution, interfacial molecular assembly has also shown increasing significance in fabricating organized thin films and devices. A direct measurement on the driving force of supramolecular self-assembly at the single-molecule level will be greatly helpful in understanding the assembly process.

2. Tuning the Amphiphilicity of Building Blocks for Controlling Self-Assembly and Dis-Assembly

An amphiphile, a molecule that contains both hydrophilic and hydrophobic parts, can self-assemble in solution or at interface to form diversified molecular assemblies, such as micelles, reversed micelles, lyotropic mesophase, monolayers and vesicles. The molecular basis of the self-assembly is the amphiphilicity. The hydrophilic part of the amphiphile is preferentially immerged in the water while the hydrophobic part preferentially resides in the air or in the non-polar solvent. The amphiphiles are aggregated to form different molecular assemblies by the repelling and coordinating action between the hydrophilic and hydrophobic parts to the surrounding environment. Since the amphiphilicity is one of molecular bases of the self-assembly, it means that if we can tune the amphiphilicity of the building blocks, we can control the process of the self-assembly to some extent. The tuning of the amphiphilicity of the building blocks, including small surfactants and amphiphilic copolymers, can be used for controlling self-assembly and disassembly.

This part is to discuss different methods for tuning the amphiphilicity, as shown in Figure 1. It contains irreversible methods that convert amphiphilic building blocks to be either hydrophilic or hydrophobic by chemical approaches. Upon transforming into non-amphiphilic, the molecular assemblies formed by the amphiphilic building blocks can be collapsed irreversibly. There are also reversible methods that can be used to tune the amphiphilicity reversibly. In this respect, reversible stimuli-responsive chemistry and supramolecular chemistry methods are involved. The conversion between the hydrophilic and hydrophobic parameters allows for the reversible self-assembly and disassembly of

the building blocks.
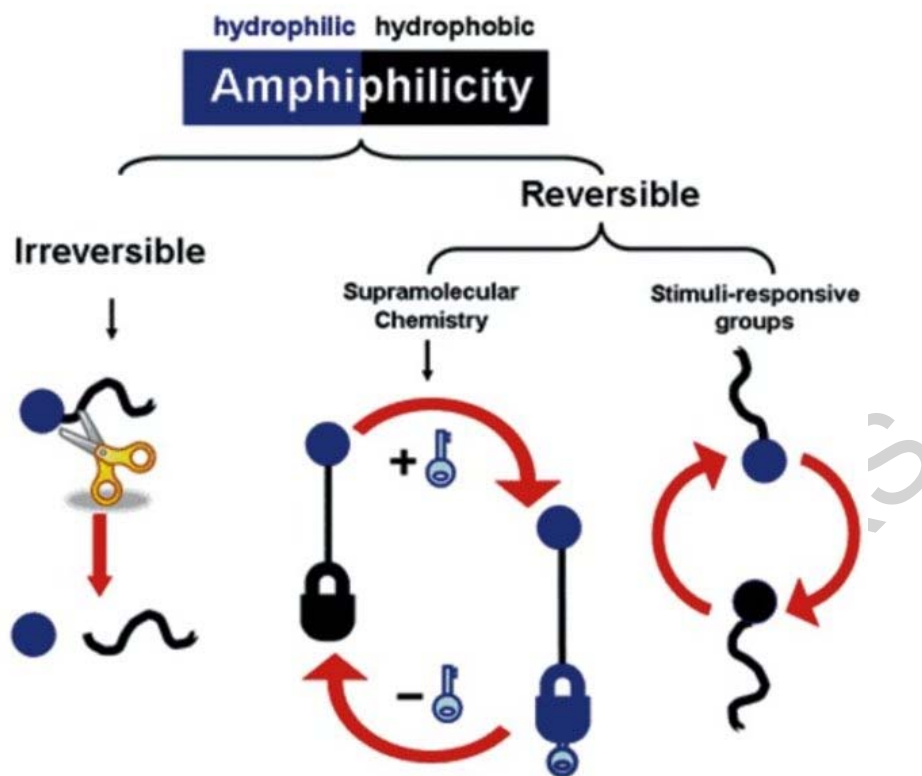
Figure1. Schematic illustration of the general methods for tuning the amphiphilicity of building blocks.

2.1. Irreversible Methods to Tune the Amphiphilicity of Building Blocks

Normally, there are two kinds of irreversible reactions used to tune the molecular amphiphilicity: the in-situ polarity variation of the special groups on the building blocks, and the detachment of the labile groups from the building blocks. In both cases, the polarity variation induced by those irreversible reactions can change the molecular amphiphilicity concomitantly, which will endow the building blocks with new properties for the application in materials science. In this part, we will discuss about how to use photo-chemical reactions, oxidation-reduction reactions, pH-stimuli reactions for tuning the amphiphilicity.

2.1.1. Photo-Irradiated Irreversible Methods

Without need of additional substances, light is one of the most desirable stimuli for tuning the molecular amphiphilicity, thus providing methods for a clean and rapid control of critical micelle concentrations (CMC), surface tensions, aggregate behavior, and types of aggregates. Ringsdorf et al employed two different photoreactions to tune the amphiphilicity of the building blocks, by which the stability of liposomal structure formed by the amphiphiles was influenced strongly. One is to tune the amphiphilicity through in-situ photoreaction on molecular skeleton. As shown in Figure 2a, the amphiphile bearing photo-sensitive head of pyridinioamidates can form lisposmes by

self-assembly in water. The photo-sensitive positive charged head on the surface of the liposome was triggered to form neutral diazepin upon UV light irradiation. The transformation of the head groups from polar to nonpolar induced the liposome to be metastable and even collapsed. This work has opened an avenue to tune the amphiphilicity of the self-assembly systems, such as micelles, liposomes, surface wettability et al. The other photo-stimuli way to vary the amphiphilicity is the detachment of photo-labile groups from the amphiphiles. As shown in Figure 2b, the amphiphilic 3,5-dialkoxybenzylammonium salts detached its hydrophilic head through UV light irradiation. Therefore, the liposome formed by such amphiphiles was deformed significantly. It should be pointed out that this line of research provides a series of photodegradative surfactants for the application in soft-lithography and separation technology.
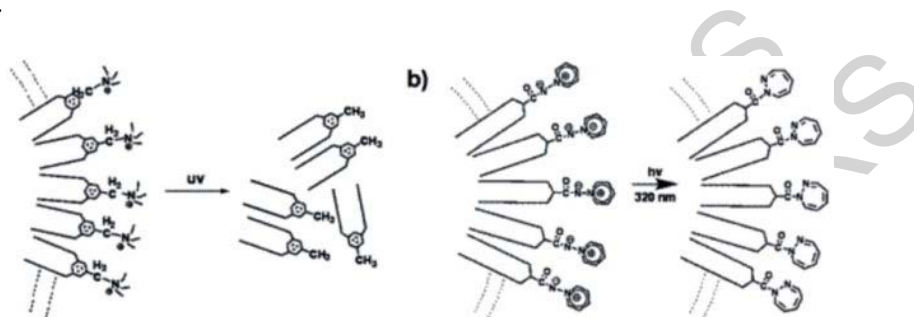
Figure 2. Photo-irradiated methods for tuning the molecular amphiphilicity: a) in-situ photoreaction of photo-responsive groups on the amphiphile; b) photolysis of photo-labile groups from the amphiphile.

Recently, a light-induced breaking of block copolymer micelles was developed by Zhao and his coworkers, which was proposed to be a model for controllable drug delivery. As shown in Figure 3, the amphiphilic block copolymer synthesized by atom transfer radical polymerization (ATRP) reaction contained photo-breakable pyrenylmethyl ester groups on the hydrophobic segment. Interestingly, the detachment of the side groups from the polymer chain by UV light irradiation induced the hydrophobic segment to be hydrophilic. This amphiphilicity variation destroyed the self-organization of the block copolymers greatly and the polymeric micelles were disassociated, which could be seen clearly by SEM observation before and after UV light irradiation. However, UV light irradiation method can hardly be clinically used in vivo because of its strong damages to the organs of human body, and it is anticipated that this concept may be developed for clinical application when UV light source could be replaced by near-infrared light (NIR).
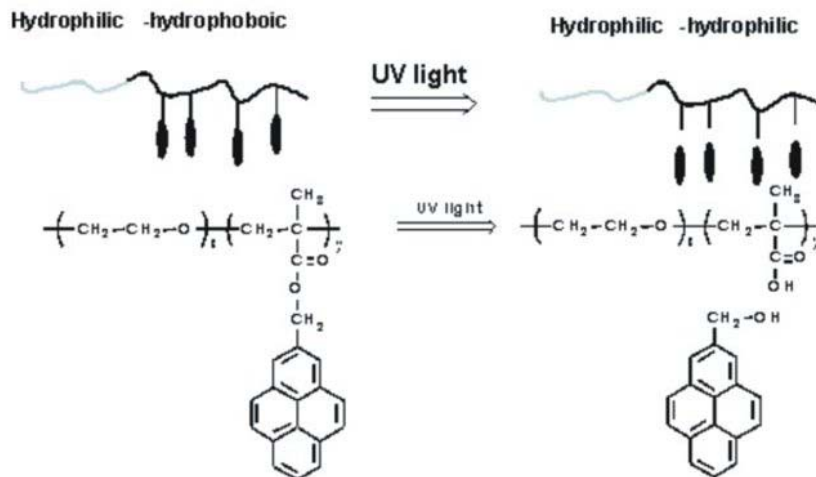
Figure 3. Photo-breakable block copolymer

2.1.2. Oxidation Reactions

As an unconventional irreversible method, oxidation reactions were also well developed to tune the molecular amphiphilicity for its potential use in drug delivery in the oxidative environment of extracellular fluids, physiologically and pathophysiologically. Usually, it is easy to understand that the oxidative reaction, with oxygen atom involved, can enhance the polarity of targeted molecules. With oxidation reaction introduced to change the polarity of some neutral or charged groups on the amphiphile, it is hoped that the hydrophilic-lipophilic balance of the amphiphile will be destroyed.
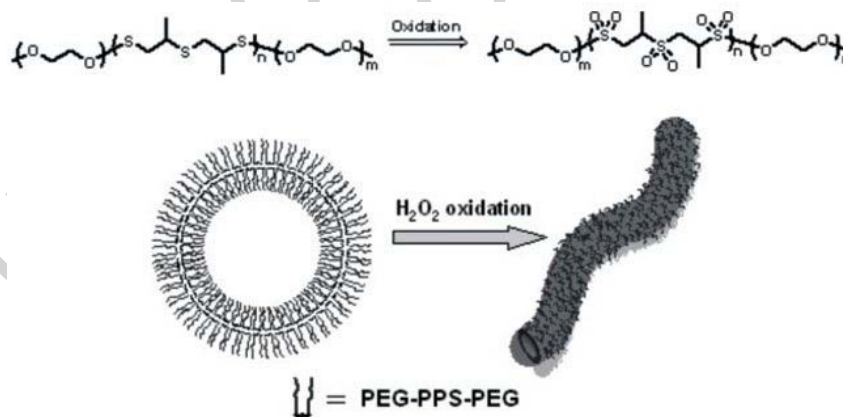
Figure 4. Oxidation-responsive copolymeric vesicles. Through the oxidation by hydrogen peroxide, the vesicles formed by triblock copolymer PEG-PPS-PEG can be transferred to worm-like micelles.

Recently, Hubbel and his coworkers designed and synthesized an ABA-type triblock copolymer as the candidate amphiphile to control the molecular self-assembly by oxidation reaction. The ABA-type triblock copolymer with hydrophilic poly (ethylene glycol) (PEG) as A-part and hydrophobic poly (propylene sulphide) (PPS) as B-part, in which PPS segment was responsive to oxidative chemicals, like H_2O_2, and it can be

converted from hydrophobic to hydrophilic upon oxidation. Rather than other poloxamer macroamphiphiles, these copolymers favored vesicle formation at room temperature without cosolvent by the greater hydrophobicity of PPS which also had a low glass transition temperature (T_g). As shown in Figure 4, in the presence of adequate H_2O_2, PPS segment was oxidized into hydrophilic sulfones and the vesicle-like aggregate were converted to long worm-like micelles. It is known that the oxidatively destabilized copolymers can be removed from the body by glomerular filtration in the kidneys, which makes this oxidative method attractive for clinical use. Later on, a very good example was proposed by encapsulating oxidant-generating enzyme glucose oxidase (GOx) into PEG-PPS-PEG triblock polymer vesicles. H_2O_2 produced by GOx-catalyzed conversion of glucose into gluoconolactone could oxidize –S- to –SO$_2$- in the PPS segment, inducing the conversion of amphiphilic triblock copolymer to a hydrophilic polymer, which will result in the breaking of the vesicle.

2.1.3. Ph-Stimuli Methods

Although increasing new stimuli-methods are being explored to tune the molecular amphiphilicity of the building blocks, pH-stimuli is still one of the most important methods based on the possibility of being used in real clinical drug delivery. The key reason for the latent use of pH-stimuli building blocks is due to the different pH condition in normal organs and tumors. In the tumor tissues in vivo, pH value drops evidently from normal extracellular physiological environment (pH 7.4) to pH 6.0–5.0, and to around pH 4–5 in primary and secondary lysosomes. This significant pH change provides great opportunities for us to develop pH-responsive systems for drug delivery. Inspired by "Ringsdorf model" in which a labile linker is introduced between drug and biocompatible polymeric backbone, many models have been created with the aim of the attachment of acid- or base-cleavable groups on amphiphiles.
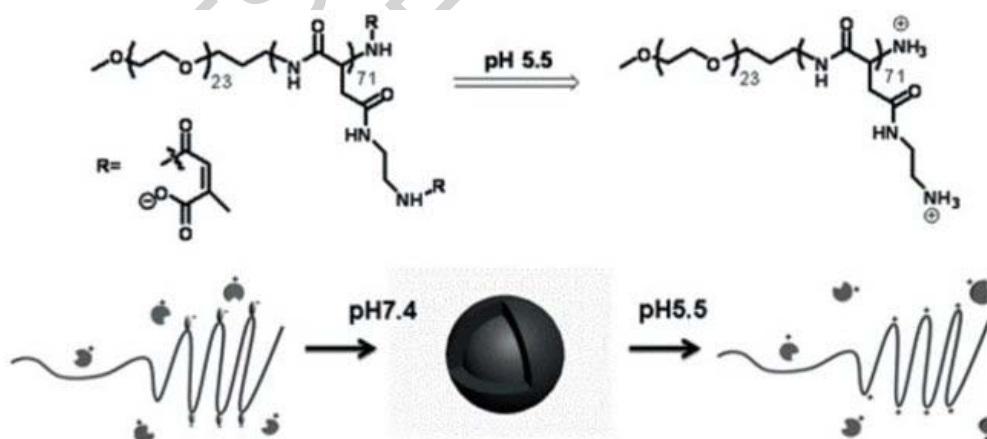

Figure 5. pH-responsive charge-conversion block copolymer poly(ethylene glycol)-poly[(*N'*-citraconyl-2-aminoethyl)aspartamide] (PEG-pAsp(EDACit)) as protein nanocarrier.

Some new and important progresses on tuning the molecular amphiphilicity and material properties by pH-stimuli need to be highlighted. For example, Kataoka and his coworkers

recently reported a pH-responsive block copolymer which can perform a charge-conversion on one block by external pH-stimuli. As shown in Figure 5, PEG-pAsp (EDACit) was a double hydrophilic block copolymer. The side comb-type citraconic amide groups endowed the pAsp block with negative charges. Therefore, this block copolymer was associated with positive-charged lysozyme based on electrostatic interaction to form poly ionic complex (PIC) type micelles. Moreover, the citraconic amide groups attached on pAsp chain were hydrolyzed through slight change of pH condition. After the hydrolysis of citraconic amide under mild condition at pH 5.5, the charge of the block copolymer changed from negative to positive. In this case, lysozyme incorporated in the micelle was repulsed and released. This active and prompt pH-stimuli response to tune the molecular amphiphilicity is promising for an effective clinical drug delivery.

Besides the wide researches on drug delivery, pH-stimulus as an easy operating method has also been explored widely in the material science. For example, through the modulation of molecular amphiphilicity, the wettability of solid surfaces could be controlled by pH-stimuli. Moreover, performing the charge-conversion on the surfaces can potentially modulate the adsorption of charged molecules on the surfaces. Recently, Zhang and coworkers designed and synthesized a bola-type amphiphile with π-conjugated dye moiety. By ionizing both terminal carboxyl acid groups, great change was observed on its aggregation morphology (Figure 6). The fiber-like aggregates could be obtained in aqueous solution when the terminal groups were in acid form. More importantly, the combination of π-π interaction among dye moieties and hydrogen bonding of the terminated groups allowed the fibers to bear a temperature as high as 130 °C, exhibiting a good thermal stability. However, the fiber structure disappeared when the carboxyl acid was converted its salt form. It is hoped that this line of research may provide an idea for controlling the self-assembly by tuning the molecular amphiphilicity which may develop biocompatible supramolecular materials with controlled morphology.

Figure 6. The AFM images of aggregation of bola-type amphiphile: a) with the terminal carboxyl acid groups; b) with the terminal potassium salt groups. Copyright 2007 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

2.2. Reversible Stimuli-Responsive Methods

There is an increasing interest in developing reversible methods, and by these methods, the molecular amphiphilicity is expected to be reversibly tuned by stimuli-responsive groups attached on the amphiphiles. By employing suitable external stimuli, those stimuli-responsive groups may change their polarity and hence the molecular amphiphilicity, but without detachment from the amphiphiles. In addition, if the change is reversible, the molecular amphiphilicity can be changeable between amphiphilicity and hydrophilicity or between amphiphilicity and hydrophobicity, providing ways to realize the control of the self-assembly.

2.2.1. Redox Switches

Since the early report on ferrocene-containing surfactant by Saji et al, diversified redox-switched groups are attracting more and more attention on their use for preparing controllable building blocks. Among those groups, ferrocene is widely used for its easy conversion between oxidized and reduced forms by electrochemistry or chemicals. Ferrocenyl surfactants, including single/double-tailed cationic surfactant and bola-amphiphile, permit the control of the formation and disruption of self-assemblies such as micelles and vesicles by redox reactions. In addition, oxidized ferrocene is stable enough to be monitored by NMR and other spectroscopic methods. Therefore, the amphiphilic molecules with ferrocene groups can be investigated well during the redox process.
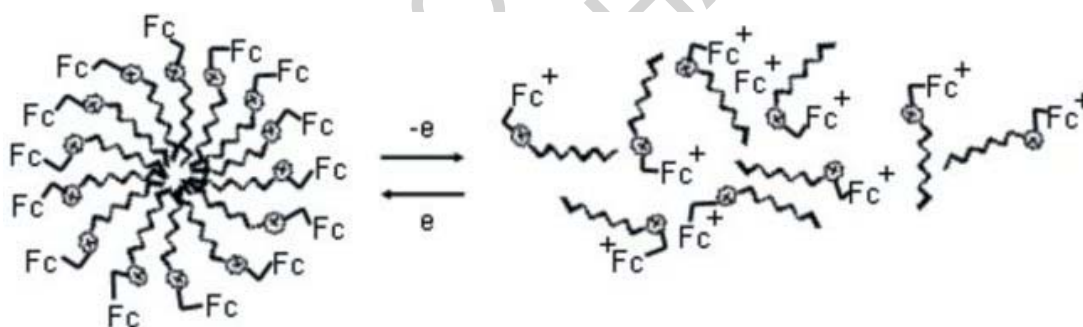
Figure 7. Controllable aggregation of ferrocene-containing surfactant by redox-stimuli.

As shown in Figure 7, the surfactant with ferrocene head group showed aggregation behavior with the concentration over its CMC. After the ferrocene groups were oxidized by oxidant, like $Ce(SO_4)_2$, the charged ferrocene groups brought better hydrophilicity to the surfactant, therefore breaking up the micelles. The property of such surfactant responding to redox-switch provides the surfactants to reversibly load small hydrophobic probes into its micelle aggregates. Later on, it was demonstrated that ferrocene-head-containing surfactant could incorporate hydrophobic small molecules to prepare organic film on electrode surface. The mechanism was that the micelles formed by surfactants with ferrocene moiety could load or disperse some sparingly water-soluble molecules onto the electrode surfaces. By electrochemical technique, the small molecules were released from the micelles onto the electrode surface, resulting in a film formation.

2.2.2. Photo-Controlled Methods

Photo-controlled method is an attractive alternative since it provides a very broad range of tunable parameters, e.g., wavelength, duration time, and intensity. Some photosensitive moieties, like azobenzene, spiropyran, stilbene, malachite green, show significant conversion between non-polar and polar reversibly through external photo-stimuli. Herein, we will discuss about how to tune the molecular amphiphilicity reversibly by introducing photo-responsive groups onto the backbone of amphiphiles.
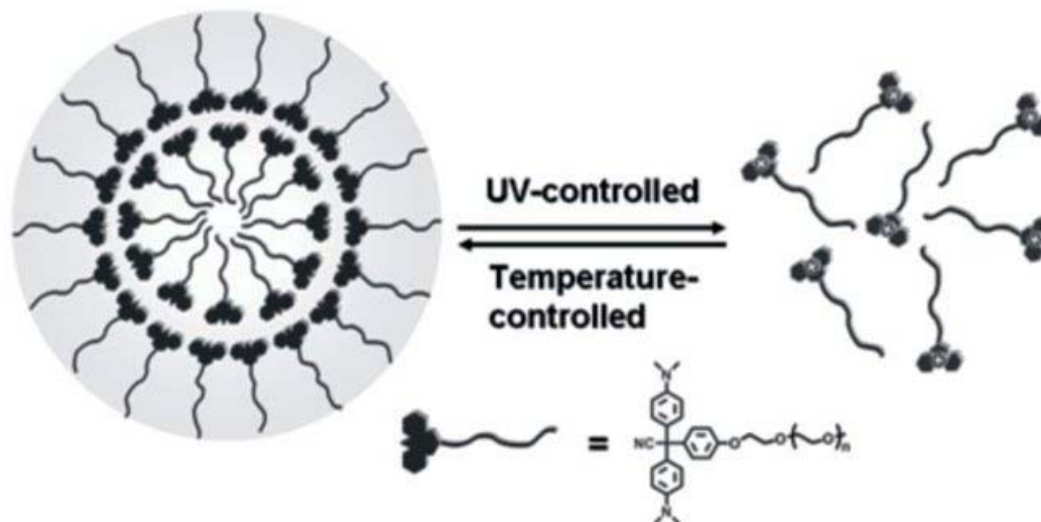

Figure 8 Reversible self-assembly of a UV-responsive Malachite green-containing amphiphile. The amphiphiles can form vesicles before UV light irradiation and the photo-induced disassembly of the vesicle takes place after UV light irradiation.

Among the various photosensitive moieties mentioned above, malachite green is of unique significance because it is hydrophobic in its neutral form, but it becomes cationic and hydrophilic upon UV light irradiation. Therefore, the introduction of malachite green into the molecular building blocks for self-assembly may lead to the development of photosensitive supramolecular systems. Recently, Zhang and coworkers have designed and synthesized some building blocks containing photo-responsive malachite green groups. Through tuning the molecular amphiphilicity by the photoreaction of malachite, the controllable assembly and disassembly of vesicles were achieved. As shown in Figure 8, the poly (ethylene glycol) (PEG)-terminated malachite green derivative showed amphiphilic property because malachite green moiety was hydrophobic in its neutral form and PEG segment is hydrophilic. As expected, this kind of amphiphilic molecules formed vesicle-like aggregates. By UV light irradiation, the color of the solution changed into deep green, indicating that the photochromic moiety of the amphiphile was ionized to its corresponding cationic form, which led to the disassembly of these vesicles. Interestingly, the cation could thermally recover to its electrically neutral form, and the disassembled species could reform amphiphiles on the basis of a thermal reverse reaction and vesicles will be reassembled spontaneously.
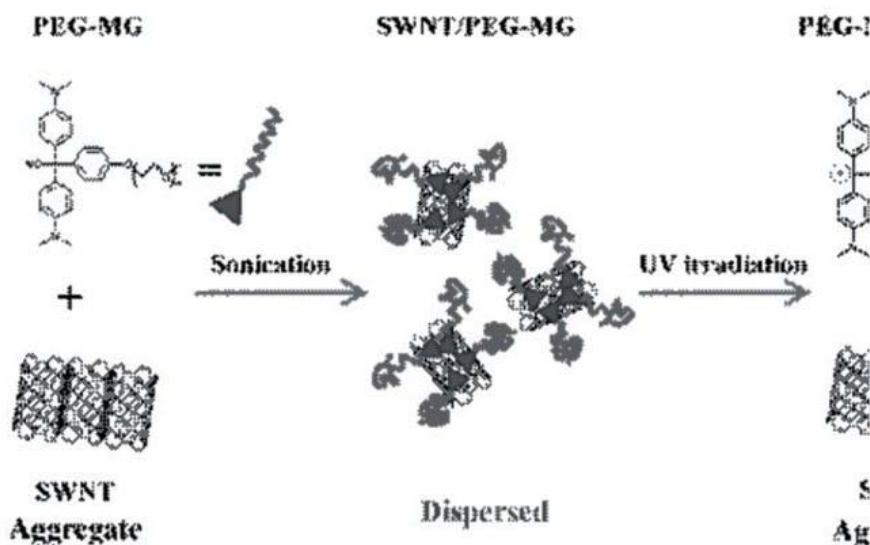
Figure 9. The use of malachite green-containing amphiphile for photo-controlled dispersion of single-walled carbon nanotubes in aqueous solution.

By using the reversible change of the amphiphilicity, the malachite green derivative can be applied to disperse single-walled carbon nanotubes in aqueous solution in a controllable way, as shown in Figure 9. Firstly, single-walled carbon nanotubes were well dispersed in aqueous solution by mixing with a certain amount of malachite green on the basis of hydrophobic and π-π interactions between the nanotube surface and amphiphilic malachite green derivative. Secondly, the carbon nanotubes could be released and precipitated in the solution after the deneutralization of malachite green groups. Here, the malachite green derivative behaved like molecular claw, wrapping carbon nanotubes and liberating them by photo-stimuli when needed. This process has a great potential use for further application of carbon nanotubes in new electronic devices and catalytic fields.

Spiropyran, another photo-responsive group, can be used to play similar games as above, since it can be switched between neutral form and zwitterionic form reversibly by alternating UV and visible light irradiation. Through the photochromatism of spiropyran, the molecular amphiphilicity of the surfactants attached with spiropyran can be well controlled. In that case, the controlled self-assembly modulation of the building blocks with spiropyran groups can be realized by light irradiation. Even more, the hydrophilic-lipophilic-balance of such kind of surfactants could be changed after photoreaction which led to the change of the surface tension. Recently, Matyjaszewski et al synthesized an amphiphilic block copolymer with poly (ethylene oxide) (PEO) as one block and poly (spiropyran) as another block by ATRP method. As shown in Figure 10, by alternating UV light and visible light irradiation, the photochromic spiropyran could be changed between neutral spiropyran (SP) form and zwitterionic merocyanine (ME). It means that the amphiphilic block copolymer PEO-b-SP could be converted to double-hydrophilic block copolymer PEO-b-ME. The micelle-like aggregates formed by PEO-b-SP were destroyed through the conversion of spiropyran to merocyanine. Moreover, the micelles could be re-formed after the recovery of spiropyran. It was also shown that the reversible micelle formation could be used to incorporate hydrophobic molecules under control.
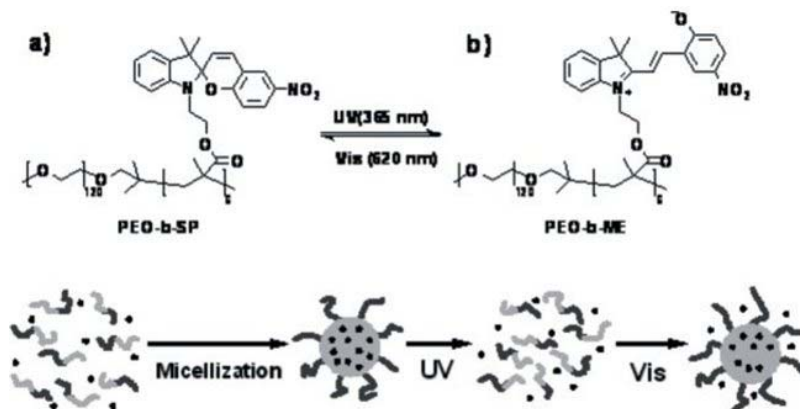
Figure 10. Light-responsive block copolymer micelle. Amphiphilic PEO-b-SP (a) can be changed to double hydrophilic PEO-b-ME (b).

The conversion of two isomers of azobenzene, trans- and cis-form, can take place reversibly by alternating UV and visible light irradiation. Azobenzene with the photo-responsive property has been applied well in material science. The change of dipole between trans-azobenzene and cis-azobenzene is estimated as 4.4 Debye, responsible for a slight polarity change between trans- and cis-azobenzene. This polarity change of azobenzene between trans- and cis-form can be amplified by attaching azobenzene groups on the polymers. Through the photoisomerization of azobenzene, the polymers or the particles with azobenzene are explored as smart photo-responsive materials, such as surface relief gratings and light-triggered bending polymer film. By introducing azobenzene group in the middle of the surfactants, the amphiphilicity can be significantly changed by light irradiation. Usually, the solubility of the building blocks will be increased after the azobenzene changes from trans- to cis-form.

2.2.3. Tuning the Amphiphilicity by Reversible Combination of Carbon Dioxide

A new approach was explored by Jessop and his coworkers to tune the molecular amphiphilicity by the combination of carbon dioxide with some specials groups. As shown in Figure 11a, before exposed to carbon dioxide, the mixture of two liquids, namely DBU (1,8-diazabicyclo-[5.4.0]-undec-7-ene) and 1-hexanol, was a non-ionic solvent. After the reaction with carbon dioxide, DBU was converted to ionic DBUH form. The mixture became an ionic liquid concomitantly. On the other way around, by exposed to enough inert gases, like nitrogen or argon, the carbon dioxide bound in the mixture could be compelled out and the mixture liquid was reversed back to be non-ionic. Very recently, based on the polarity conversion, this kind of solvent was employed to dissolve the reagents for a chemical synthesis and then precipitate the product under control. For example, the monomer styrene dissolved well in non-polar solvent could be polymerized to polystyrene. Through the exposure of system to carbon dioxide, the polymer could not be dissolved in polar solvent anymore and instead, it deposited on the bottom of the container. In addition, the solvent could be used repeatedly through removing carbon dioxide by nitrogen or argon. Therefore, this carbon dioxide involved method is considered as a green concept to tune the amphiphilicity because only harmless and cheap gases are used in the system.
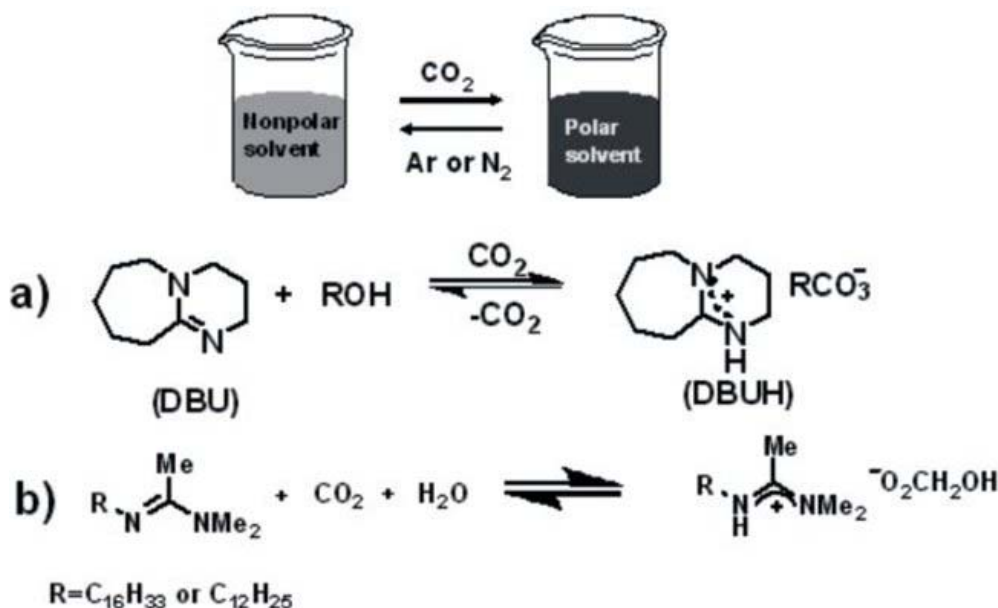
Figure 11. a) The carbon dioxide switchable solvent. By the combination of carbon dioxide with DBU, the non-polar mixture of DBU and hexanol can be changed to be a polar ionic liquid. This polarity change will be reversed by nitrogen gas, which could stripe out the carbon dioxide from the mixture. b) A carbon dioxide-responsive switchable surfactant. By reacting with carbon dioxide, the neutral alkyl amidine can be converted to amphiphilic amidinium bicarbonate salt with an alkyl chain.

On the basis of a similar concept, as shown in Figure 11b, Jessop et al designed and synthesized other kinds of compounds bearing carbon dioxide-responsive long-chain alkyl amidine groups that could be reversibly transformed into charged surfactants by exposure to an atmosphere of carbon dioxide. The cationic surfactants were proven to be effectively used for stabilizing water/alkane or oil emulsions, and the microsuspension polymerization. Taking crude oil as a test example, the mixture of water and oil could form a fairly stable emulsion in the presence of the cationic surfactants, being separated into two layers after enough argon treatment. It is well known that carbon dioxide is easily achievable from the atmosphere, thus the amphiphilicity control of building blocks by exposure to carbon dioxide is anticipated for potential industrial application, such as the separation of oil from oil sands, the transportation of oil emulsion through the pipelines, and then the release of oil when needed.

2.3. Supramolecular Methods

Supramolecular chemistry concerns molecular assemblies and non-covalent interactions. The reversibility of non-covalent interactions used in supramolecular chemistry, like hydrogen-binding, π-π interaction, Van der Waals force, host-guest interaction, metal-ligand coordination, endows the assemblies with stimuli-responsive ability. Herein, the main idea is how to construct supramolecular amphiphiles that are formed on the basis of non-covalent interactions. The supramolecular amphiphiles refers to supramolecules of two component systems: one is a host amphiphile non-covalently binding with a guest molecule; the other is a non-amphiphilic building block binding with a hydrophilic guest.

By changing the non-covalent interactions, the amphiphilicity of those supramolecular amphiphiles can be tunable between more hydrophilic and less hydrophobic or between more hydrophobic and less hydrophilic. Therefore, the supramolecular amphiphiles are hoped to display controlled aggregation behaviors and new functions.

2.3.1. Hydrogen Bonding Method

The use of complementary hydrogen bonding for fabricating supramolecular amphiphiles dates back to the early work of Kunitake et al who employed substituted melamines as hydrogen acceptor and isocyanuric acid derivatives as hydrogen donor. As shown in Figure 12, sparingly water-soluble (1) and (2) with hydrogen donor groups were used as guest building blocks. They both can bind with the host hydrogen acceptor-containing amphiphiles (3) and (4) on the basis of hydrogen bonding interaction to form supramolecular amphiphiles. Through the combination with hydrogen acceptor, the amphiphilicity of amphiphilic hydrogen donor can be changed greatly because the hydrophobic segment was elongated. However, the hydrogen bonding interaction was weakened in polar water and the supramolecular amphiphile could not be formed by mixing hydrogen donor and acceptor directly. To prepare the supramolecular amphiphiles, the authors dissolved the hydrogen donor and acceptor in a cosolvent ethanol and removed the solvent to form a solid-state mixture. After repeating this cycle three times, the final product was dissolved in water. Different from the single amphiphiles, the supramolecular amphiphiles could form disk-like aggregates, which was confirmed as a bilayer structure. By changing the alkyl length of hydrogen acceptors, the supramolecular amphiphiles displayed a different aggregation behavior. Since the strength of hydrogen bonding interaction depended on applied temperature, the bilayer structure of the aggregates formed by the supramolecular amphiphiles could be thermally dissociated reversibly. The concept of this family of hydrogen bonding-based supramolecular amphiphiles opens an avenue to fabricate new supramolecular amphiphiles on the basis of hydrogen bond.
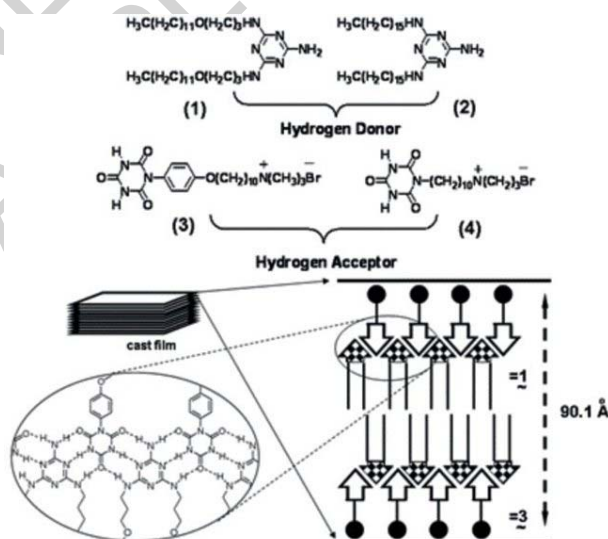

Figure 12. Supramolecular amphiphiles based on hydrogen bonding interaction. In the cast film, the supramolecular amphiphiles dominantly form bilayer structure.

2.3.2. Charge-Transfer Interaction

Charge-transfer interaction between electron donor and acceptor is developed as a new non-covalent force for the fabrication of supramolecular assemblies. Very recently, Zhang and coworkers established a supramolecular system for the modulation of self-assembly through the weak charge-transfer interaction. As shown in Figure 13, an amphiphilic electron donor PYR and a hydrophobic electron acceptor DNB were involved for the formation of charge-transfer interaction based supramolecular amphiphile. The amphiphilic PYR itself could form tube-like aggregates with the concentration over its CMC (TEM image, Figure 13a). By the method mentioned in Kunitake's work, dissolving-drying three times, a mixture of PYR with DNB could be obtained. Interestingly, this supramolecular amphiphile formed stable vesicles in water. It was clearly evidenced that the introduction of charge-transfer interaction into the supramolecular assembly could induce the transformation of the aggregates from tube-like to be vesicle-like. This morphology transformation is understood by the curvature change of the aggregates through the introduction of charge-transfer interaction. This line of work may exemplify the enormous potential of self-assembly for the construction of well-defined nanostructures by controlling the amphiphilicity of building blocks.

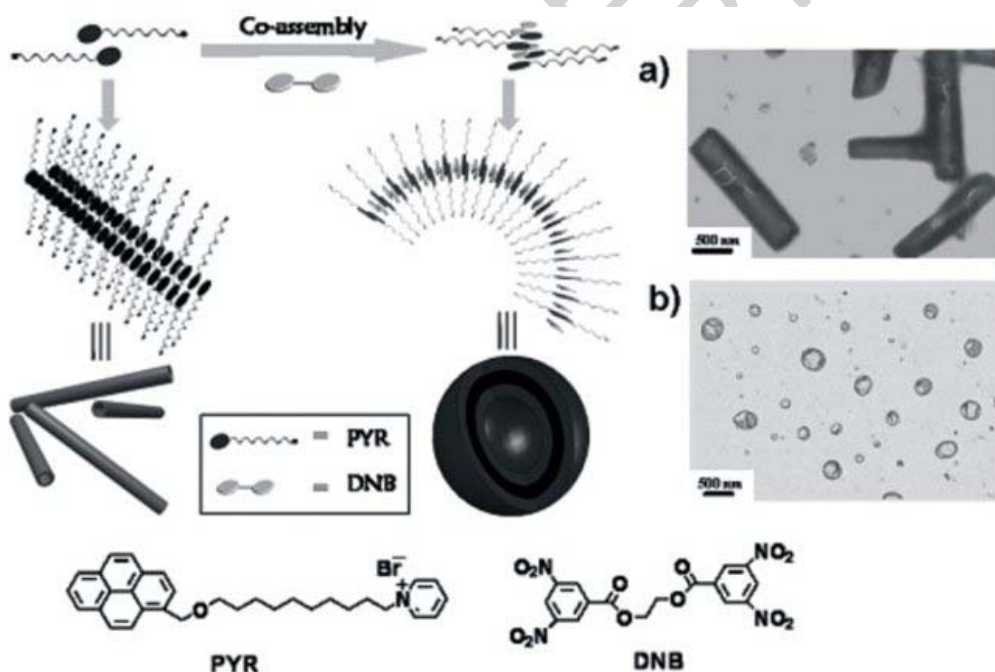Figure 13. The transformation of tube-like aggregates to vesicles modulated by charge-transfer interaction. Copyright 2008 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

2.3.3. Host-Guest Modulation Employing Cyclodextrin as Host

Among so many supramolecular host-guest systems, some host molecules as building blocks can implant other building blocks which are employed as the guest in their bodies.

Till now, some hosts are well investigated, including cyclodextrins, crown ethers, cucurbiturils, calixarenes, etc. In this section, we present some successful examples about tuning the amphiphilicity through the introduction of cyclodextrin.

Cyclodextrin (CD), which is divided into α-CD, β-CD, and γ-CD, is mainly formed by the bridge-linking of glucose units. CD can be dissolved in water very well because of the water-soluble nature of outer surface and it provides a hydrophobic cavity resulting from the water-insoluble interior. This series of host molecules can precisely bind with many kinds of small hydrophobic molecules depending on the complementarity of size and shape. Based on this reason, cyclodextrin has been explored well as water-soluble nanocontainer and reactor. Stoddart, Harada, and Wenz et al one after the other reviewed some works about the utilization of CDs as building ring to fabricate rotaxane-like supramolecular assemblies through the self-assembly of CDs with amphiphiles. Usually, two possibilities are expected when cyclodextrin binds with a guest molecule. If the guest is sparingly water-soluble, it will become a supramolecule amphiphile by binding with cyclodextrin because the cyclodextrin can function as a hydrophilic head. For a normal amphiphile, it can bind well with CD through the interaction between CD and the alkyl chain. This host-guest interaction can increase the solubility of the hydrophobic chain and change the amphiphilicity, which results in the disruption of the aggregates of the amphiphiles.

One of the interesting examples with the regard to the use of cyclodextrin for tuning molecular amphiphilicity was reported by Kim et al. They synthesized a dendritic amphiphile with a focal pyrene group. This dendron amphiphile formed vesicles in aqueous solution. Interestingly, upon addition of β- or γ-CD, the association of pyrene group with CD changed the amphiphilicity of the amphiphile and induced the vesicle aggregates to be converted into tube-like aggregates. When CDs were removed from the amphiphiles by poly (propylene glycol), the vesicle-like aggregates could be regenerated very well.

It is well known that the host-guest interaction between azobenzene and α-CD or β-CD can be controlled through the photoisomerization of azobenzene. Recently, Zhang and coworkers have taken this unique feature and presented a concept of combining host-guest chemistry and photochemistry to tune the amphiphilicity (Figure 14). In our work, an azobenzene-containing surfactant was used which could form vesicle-like aggregates in aqueous solution. The enhanced water-solubility by the binding of α-CD with azobenzene disrupted the vesicles remarkably. After the photoisomerization of azobenzene from trans- to cis-form by UV light irradiation, α-CD could not bind with azobenzene any more and slid onto the alkyl chain. This movement of α-CD changed the amphiphilicity of the supramolecular amphiphile and new aggregates were formed subsequently, whose size was smaller than that by pure amphiphiles. When azobenzene recovered to its trans-form by visible light irradiation, α-CD moved back onto azobenzene group and induced the disruption of the aggregates again. An interesting finding was that the shuttle-like movement of α-CD on the amphiphile could tune the aggregation behavior reversibly through the photoisomerizaiton of azobenzene.
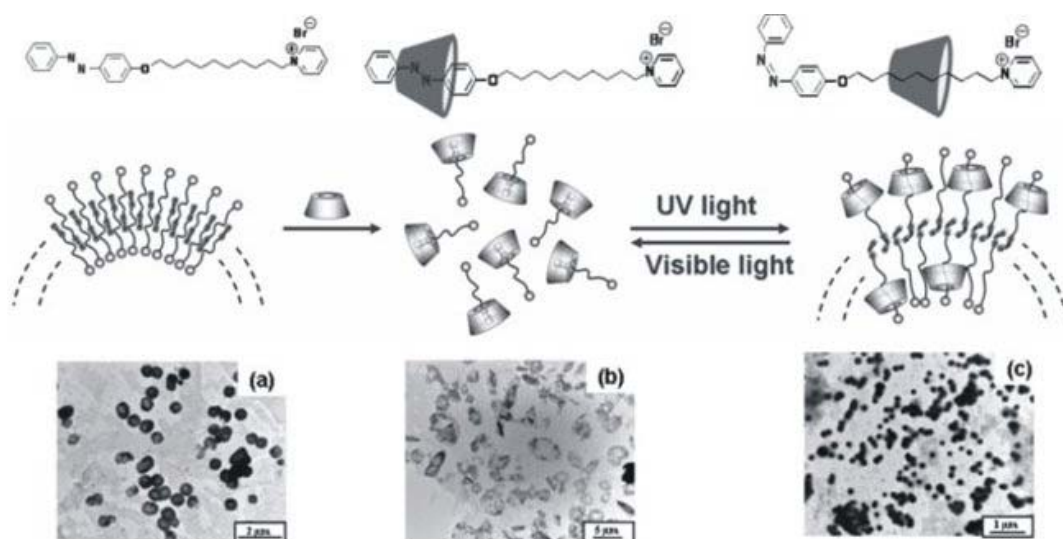
Figure 14. Photocontrolled reversible supramolecular assembly of azobenzene-containing surfactant with α-CD. a) vesicles formed by the pure amphiphiles; b) the destruction of the vesicles by the introduction of α-CD; c) new aggregates formed when α-CD slides onto the alkyl chain by UV light irradiation. Copyright 2007 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

As mentioned, the movement of cyclodextrin can induce the amphiphilicity change of the guest molecule, thus we have the reason to believe that the surface modified with such rotaxane-like assemblies can display different wettability upon the movement of cyclodextrin. Very recently, Zhang and coworkers fabricated this kind of molecular shuttle onto rough gold substrate by SAM, whose wettability could respond to the photo-stimuli. In this work, an azobenzene-containing building block with a mecapto-group at the end preassembled with α-CD in water based on the interaction between azobenzene and α-CD, forming a sort of supramolecular amphiphile (Figure 15). This supramolecular amphiphile could form a mixed SAM with n-butylthiol on gold substrate. The purpose of fabrication of the mixed SAMs was to ensure that there was enough free space for the movement of the molecular shuttle. Before UV light irradiation, α-CD stayed on the top of the surface and the SAM displayed hydrophilic property. After UV light irradiation, α-CD slid down onto the alkyl chain and the SAMs became hydrophobic. Nearly 50 ^{o} change for the surface contact angle with a water droplet as an indicator was found before and after UV light irradiation. This great change of wettability could be cycled several times by the alternating UV and visible light irradiation. The shuttle movement mechanism of α-CD on this SAM was well supported by cyclic voltammetry study. Because of the good biocompatibility of cyclodextrin, it is anticipated that this light-driven surface can be developed as bio-devices for controllable cell adsorption.
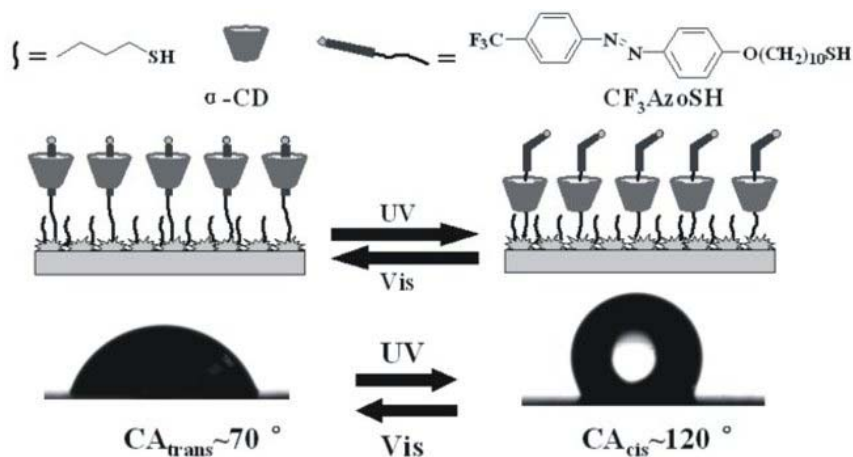
Figure 15. Photo-responsive self-assembled monolayer with the molecular shuttles. When cyclodextrin stays on the azobenzene group, the contact angle is around 70 °, indicating surface is hydrophilic; when cyclodextrin slides onto the alkyl chain, the contact angle becomes 120 °, indicating the surface is hydrophobic.

2.3.4. Host-Guest Modulation Employing Cucurbituril as Host

Cucurbituril is another interesting host molecule, with a similar hydrophobic cavity to cyclodextrin, which can be used to incorporate guest molecules. It has been explored very well as building blocks for supramolecular assembly both in solutions and on solid surfaces. Kimoon et al presented an early example by combining the host-guest chemistry with charge-transfer interaction to form a supramolecular amphiphile in aqueous solution. The surfactants with bipyridium groups themselves formed micelles in aqueous solution. Interestingly, in the presence of cucurbituril, the electron acceptor of bipyridium group and the electron donor of dihydroxynaphthalene could form a pair in the cavity of cucurbiuril based on the charge-transfer interaction. This supramolecular amphiphile displayed new aggregation behavior in water and formed vesicle-like aggregates as observed by TEM. Upon addition of oxidative chemicals, like cerium(iv) ammonium nitrate, the electron donor of dihydroxynaphthalene was oxidized and the supramolecular assemblies based on charge-transfer interaction could be collapsed.
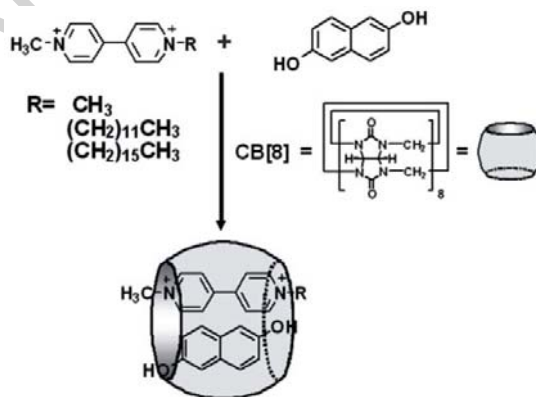

Figure 16. Supramolecular amphiphile formation based on the charge-transfer interaction in a host.

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Biographical Sketches

Huaping Xu was born in Jiangsu, China in 1978. He received his Bachelor degree in 2001 and Ph. D. degree in 2006 in polymer chemistry and physics at Jilin University, China, under the supervision of Prof. Xi Zhang. During 2004-2005, he worked as an exchange Ph. D. student in University of Leuven, Belgium. In 2006, he joined Prof. David N. Reindhout and Prof. Jurriaan Huskens's group at University of Twente, the Netherlands, as a post-doc. Since 2008, he is a lecturer at the Department of Chemistry, Tsinghua University, China. His current research interests are focused on supramolecular assembly and functional polymers.

Xi Zhang was born in Hunan, China in 1965. He received his B.S. degree in 1986 at Department of Chemistry, Jilin University, China. He received his M.S. degree and Ph.D in 1989 and 1992 respectively in polymer chemistry and physics at the same university. As a joint-training Ph.D student, he worked with Prof. Helmut Ringsdorf, University of Mainz, Germany, between 1991 and 1992.

He became a full professor of Jilin University in 1994 and director for the Key Lab of Supramolecular Structure and Materials in 1997. Since 2003, he is a full professor of the Department of Chemistry, Tsinghua University, Beijing. Currently, he is appointed as Department Chair. His research interests are focused on supramolecular assembly and polymer thin films, single molecular force spectroscopy of polymers.

Prof. Zhang serves as Senior Editor of Langmuir and Editorial Board Members of several scientific journals, including Chemical Communications, European Polymer Journal, and ACS Applied Materials and Interfaces. He has been a member of Chinese Academy of Sciences since 2007.

Junqi Sun was born in Shangdong Province in 1975. He received his BS and PhD degrees in 1996 and 2001, respectively at Jilin University, majoring in polymer chemistry and physics. His Ph. D thesis work, under the direction of Prof. Jiacong Shen and Prof. Xi Zhang, investigated the construction and

functionalization of layered ultrathin films. Between January of 2002 and August of 2003, he joined in Prof. Toyoki Kunitake's group at RIKEN as a Postdoctoral Fellow. In September of 2003, he joined the faculty of Jilin University as a professor of Chemistry. In 2003, he won the prize for the Author of National Excellent Doctoral Dissertation of P. R. China. He is also the winner of the Chinese Chemical Society Prize for Young Scientists in 2007. His main research interests focuses on the fabrication of polymeric and polymeric/inorganic hybrid films and their functionalization.

Shuxun Cui was born in Hebei, China in 1977. He received his BS and PhD degrees in polymer chemistry and physics at Jilin University under the supervision of Prof. Xi Zhang in 1999 and 2004, respectively. After the doctoral research, he joined the group of Prof. Hermann E. Gaub in the University of Munich for one year as a Humboldt Fellow. In 2005, he joined the Sichuan University in Chengdu, China as an Associate Professor. Three years later, he moved to the Southwest Jiaotong University in the same city as a Full Professor. His current research interest involves the single-molecule mechanics and self-assembly of biomacromolecules.

Prof. Cui is the member of the Chinese Chemical Society and Chinese Materials Research Society.