論文の内容の要旨

Self-Assembly of Conical Fullerene Amphiphiles and Their Behavior at Air-, Oil-, and Solid-Water Interfaces

(両親媒性コニカルフラーレンの自己集合とその気液，液液，
および固液界面における挙動)

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1. Introduction

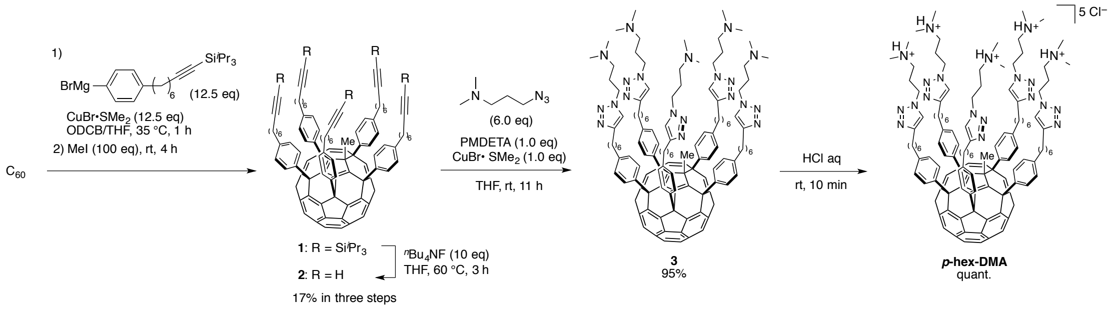
Surfactants lower the interfacial tensions between air, liquid and solid, and form micelles in water, and thereby are used as detergent, foaming and wetting agent, dispersion agent etc. Suppression or enhancement of one function over others is often necessary but difficult, because of the structural flexibility of surfactants and the ensuing paucity of information on the structure-activity relationship. Apart from the conventional alkyls surfactants, researchers have developed a variety of amphiphiles that consist of rigid or dendritic moieties. However lack of systematic study on their surfactant properties impaired versatility of the novel systems. To develop a series of amphiphiles that enable tuning of the functions, I focused on [60]fullerene. The chemical reactivity of fullerene has afforded a variety of amphiphiles that show unique properties.

In my doctoral course, I focused on compact, conical fullerene amphiphiles (CFAs) whose structure can be modified easily without much affecting the molecular shape. Conical fullerenes have well-defined structures that can be easily synthesized by pentaaddition reaction. Introduction of multiple hydrophilic groups to the framework structure affords high water solubility required for practical use of surfactants, without deteriorating the cohesive power of fullerene. Herein I proposed that CFAs prefer micellization rather than adsorption to air- and oil-water interfaces, and showed their applicability in DNA compaction and solid dispersion. Use of click reaction enabled to synthesize a series of water-soluble amphiphiles that can micellize and compact DNA into nanoparticles effectively. Interfacial activity of nonionic CFAs can be retarded by changing the molecular geometry. The systematic study on ionic and nonionic CFAs showed that ionic CFAs can specifically act as dispersion agents for solid nanoparticles.

2. Results and discussion

Aminofullerenes are known to compact DNA and thus are applicable for transfection. The effectiveness is expected to be improved by increasing the number of amino groups. In addition, a linker that is easily formed between hydrophilic functional groups and the fullerene-based hydrophobic entities is needed to develop a series of fullerene amphiphiles for systematic study. To remedy these issues, I have designed a modular synthetic route to a new CFA (***p*-hex-DMA**) via click cycloaddition chemistry (Scheme 1), and examined its behavior in micelle formation and DNA binding.

Scheme 1. Synthesis of ***p*-hex-DMA**



The conical fullerene amphiphile (CFA) bearing five cationic groups shows high solubility in water to form micelles of ca. 12 nm in diameter at low critical micelle concentration (CMC) of 3.6 ± 0.5 μM (Figure 1a). The micelle of ***p*-hex-DMA** forms a structurally defined stable complex with DNA in a buffer solution. Upon mixing with a double stranded DNA, it forms reproducibly a spherical aggregate of 50-nm diameter at a N/P ratio (the ratio between amino groups of CFA and phosphate groups of DNA) as small as 0.5–1 in a hepes buffer (Figure 1b). This diameter of the fullerene/DNA aggregate was previously shown to be useful for gene delivery across cell membrane.

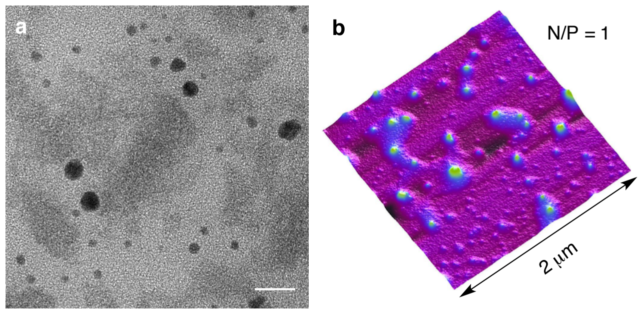


Figure 1. Microscopic observation of nanostructures formed by the cationic CFA. (a) Micelles of ***p*-hex-DMA** on amorphous carbon film observed by scanning transmission electron microscopy (STEM) and (b) the CFA/DNA complex on mica observed by atomic force microscopy (AFM). Scale bar is 20 nm.

3. Conclusion

In this thesis, I have shown synthesis, surfactant properties, and application of CFAs. ***p*-hex-DMA** forms a stable micelle in water and in a buffer at low CMC. The N/P ratio =1 needed for efficient DNA compaction is expected to render this new aminofullerene a transfection agent with minimum side effects. I have shown that CMC of nonionic CFAs can be lowered than the concentration where interfacial tension drops by tuning molecular geometry of the CFA framework. Ionic CFAs do not have interfacial activity at air- and oil-water interfaces, while they serve as efficient dispersion agents for solid materials. The systematic study on structure-activity relationship of the fullerene amphiphiles will enable us to expand the utility of fullerene amphiphile to practical use such as delivery of drug molecules including nucleic acids, or nanoparticles by use of minimal amount of surfactants, or as dispersants for formulation of cosmetics and pigments that show effectiveness without causing foaming.