

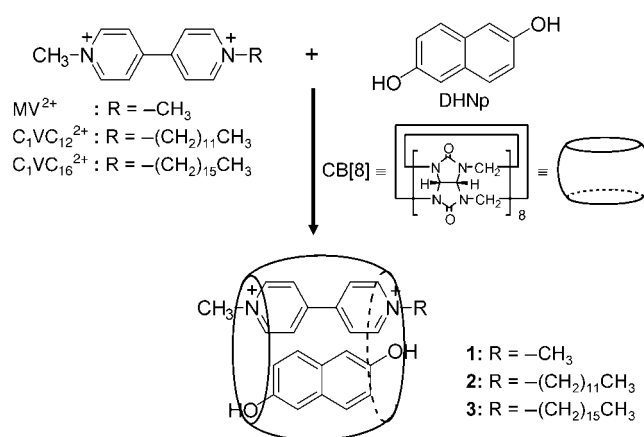
# Supramolecular Amphiphiles: Spontaneous Formation of Vesicles Triggered by Formation of a Charge-Transfer Complex in a Host\*\*

Young Jin Jeon, Parimal K. Bharadwaj, SooWhan Choi, Jae Wook Lee, and Kimoon Kim\*

Studies on vesicles have received much attention in recent years as they are important building blocks of all living systems and are potentially useful in many areas of chemistry, biology, and material science: for example, in the development of light-harvesting systems, artificial ion channels, drug/gene delivery systems, and new smart materials.<sup>[1–3]</sup> Over the last decade a wide variety of synthetic amphiphiles with different polar head groups and hydrophobic tails have been reported.<sup>[2,3]</sup> With only a few exceptions,<sup>[4]</sup> however, these amphiphiles are single molecules prepared by conventional covalent synthesis. Herein we report, for the first time, the spontaneous formation of giant vesicles triggered by the formation of a stable ternary inclusion complex that behaves as a large supramolecular amphiphile. Furthermore, the disruption of the vesicles can be easily triggered by a redox process.

Cucurbit[6]uril (CB[6]), a macrocyclic cavitand comprising six glycoluril units, has a hydrophobic cavity that is accessible through two identical carbonyl-fringed portals. It has been widely used as a synthetic receptor<sup>[5,6]</sup> and as a building block for supramolecular architectures.<sup>[7]</sup> Our recent synthesis of new cucurbituril homologues,<sup>[8]</sup> cucurbit[*n*]uril (CB[*n*], *n* = 5, 7, and 8) containing five, seven, and eight glycoluril units, respectively, has opened up new opportunities in supramolecular chemistry.<sup>[9,10]</sup> For example, CB[8], which has a cavity comparable to that of  $\gamma$ -cyclodextrin, can form a stable 1:1:1 complex (**1**) with methyl viologen (MV<sup>2+</sup>) and 2,6-dihydroxynaphthalene (DHNp) (Scheme 1).<sup>[9a]</sup> The formation of the ternary complex is driven by charge-transfer interaction between the electron-deficient and electron-rich guest molecules inside the hydrophobic cavity of CB[8]. This discovery prompted us to explore supramolecular assemblies of higher hierarchy based on formation of a ternary complex.

Sonication of an equimolar mixture of CB[8], a viologen with a C<sub>12</sub> or C<sub>16</sub> alkyl chain (C<sub>1</sub>VC<sub>12</sub><sup>2+</sup> or C<sub>1</sub>VC<sub>16</sub><sup>2+</sup>, respectively),<sup>[11]</sup> and DHNp in water results in a transparent



Scheme 1. Formation of stable ternary complexes **1**, **2**, and **3**.

or turbid solution with a violet color corresponding to **2** and **3**, respectively.<sup>[12]</sup> A broad absorption band centered at about 550 nm in their UV/Vis spectra,<sup>[13]</sup> as in **1**, indicates the formation of charge-transfer complexes inside CB[8] (Scheme 1). Without CB[8], binary mixtures of C<sub>1</sub>VC<sub>12</sub><sup>2+</sup> (or C<sub>1</sub>VC<sub>16</sub><sup>2+</sup>) and DHNp do not produce any color change, which supports the theory that these charge-transfer complexes are indeed formed inside the CB[8] cavity. Conclusive evidence for the formation of stable 1:1:1 ternary complexes were further obtained from <sup>1</sup>H NMR and ESI mass measurements.<sup>[12]</sup> For example, in the <sup>1</sup>H NMR spectrum of **2**, the signals for the bipyridinium unit of C<sub>1</sub>VC<sub>12</sub><sup>2+</sup> and DHNp shift up-field, whereas those for the alkyl tail of C<sub>1</sub>VC<sub>12</sub><sup>2+</sup> (particularly those for the methylene units close to the bipyridinium unit) shift down-field relative to those in their free forms. This observation is consistent with the formation of a charge-transfer complex between the bipyridinium unit of C<sub>1</sub>VC<sub>12</sub><sup>2+</sup> and DHNp inside CB[8], and the presence of a signal at *m/z* 914.30 [*M*<sup>2+</sup>] in the ESI mass spectrum exactly matching the formula mass of **2** (*m/z* 942.86 for **3**) further confirms the formation of a ternary complex.

Most interestingly, the ternary complexes **2** and **3** form large vesicles, which has been confirmed by light microscopy, TEM, and SEM measurements.<sup>[13]</sup> The TEM images (Figure 1a) of **2**, which has a C<sub>12</sub> hydrophobic tail, reveal nearly monodispersed vesicles with an average diameter of 20 nm. On the other hand, **3**, which has a C<sub>16</sub> hydrophobic tail, forms relatively large vesicles with a diameter ranging from 20 nm to 1.2  $\mu\text{m}$  (TEM images, Figure 1b). A high-resolution TEM image of the vesicles<sup>[13]</sup> shows their hollow structures. Dynamic light scattering data of **3** in water indicate the presence of supramolecular aggregates with an average diameter of 870 nm. The SEM images (Figure 1c) of **3** also show large spheres with a diameter ranging from 20 nm to 1.2  $\mu\text{m}$ ; the typical vesicle size lies between 400 and 950 nm. The SEM images also demonstrate that the vesicles are robust as they maintain the spherical shape even when they are dried on a solid surface. This observation is in sharp contrast to most vesicle systems made of natural or synthetic amphiphiles, which are flattened on a surface under similar conditions.<sup>[2a]</sup> The origin of the extraordinary stability of the present vesicles is, however, not yet clear. We must point out that C<sub>1</sub>VC<sub>12</sub><sup>2+</sup>

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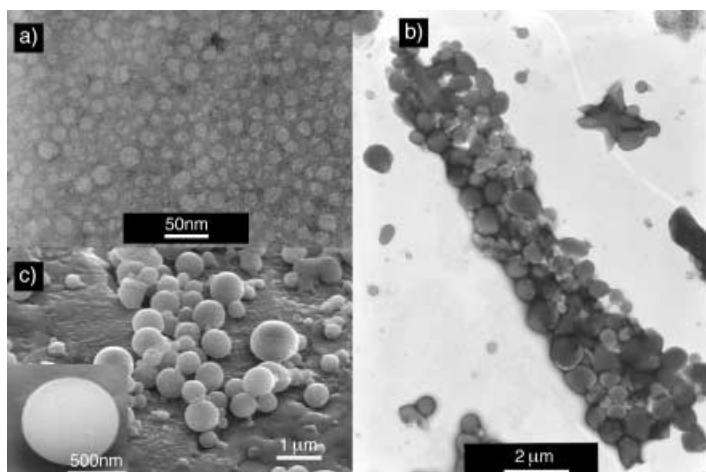


Figure 1. a) TEM image of ternary complex **2**. b) TEM image of ternary complex **3**. c) SEM image of ternary complex **3**. Samples (concentration =  $6.9 \times 10^{-4}$  M) were negatively stained with uranyl acetate (2 wt % in water) for observation by TEM.

and  $C_1VC_{16}^{2+}$  itself form only micellar aggregates at the same concentration ( $6.9 \times 10^{-4}$  M, critical micelle concentration (cmc) = ca.  $1 \times 10^{-4}$  M).<sup>[14]</sup> Therefore, the formation of vesicles is triggered by the formation of the ternary complexes CB[8]-DHNp- $C_1VC_{12}^{2+}$  (or  $C_1VC_{16}^{2+}$ ), which behave as supramolecular amphiphiles with a large polar head group and a hydrophobic tail. Such spontaneous formation of vesicles triggered by the formation of a ternary complexes is unprecedented.

Further evidence for the formation of vesicles of **2** and **3** is provided by encapsulation of the fluorescent dye sulforhodamine G (**S**) within the interior of the vesicles. Figure 2 (inset) is a representative fluorescence microscopy image of **3**, which has been prepared in the presence of **S** and purified by dialysis, and shows the entrapment of **S** in the vesicle **3**. The stability of the vesicles is also demonstrated by very slow release of the fluorescent dye trapped inside the vesicles (Figure 2). Addition of Triton X-100, which is known to solubilize vesicles, triggers a quick release of the dye. The dye-entrapment experiment, which is known to provide a clue to the lamellarity of vesicles,<sup>[15]</sup> suggests that the vesicle **3** is unilamellar rather than multilamellar.<sup>[13]</sup>

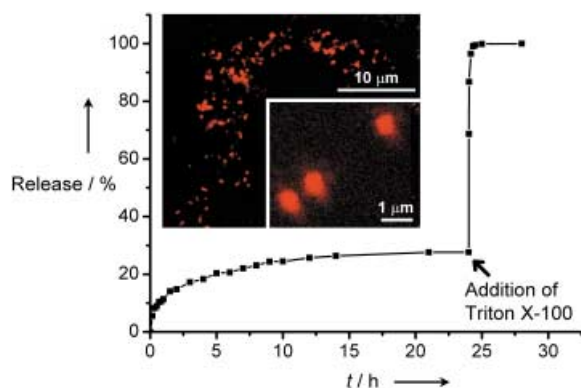


Figure 2. Confocal fluorescence microscope images of vesicle **3** containing entrapped sulforhodamine G (inset) and release profile of the dye from the vesicle.

The two components, DHNp and  $C_1VC_{12}^{2+}$  (or  $C_1VC_{16}^{2+}$ ), which reside inside the cavity of CB[8] in **2** (or **3**) are redox active. Therefore, we anticipated that oxidation of DHNp or reduction of  $C_1VC_{12}^{2+}$  (or  $C_1VC_{16}^{2+}$ ) would result in destruction of the ternary complex as a result of the loss of charge-transfer interaction between the two guests, which may in turn cause collapse of the vesicles. With this idea in mind, we treated **2** and **3** with cerium(IV) ammonium nitrate (CAN) which can oxidize DHNp to naphthoquinone. The charge-transfer band at 550 nm disappears in the UV/Vis spectrum of **2** or **3** upon treatment with CAN which indicates destruction of the charge-transfer complex inside CB[8].<sup>[13]</sup> The collapse of vesicles of **3** has been confirmed by SEM; the previously observed spherical objects no longer exist in the SEM images of the CAN-treated sample.<sup>[16]</sup> We are currently exploring other methods to disrupt the vesicles under mild conditions.

In conclusion, we have demonstrated the spontaneous formation of giant vesicles triggered by formation of a stable ternary inclusion complex that behaves as a large supramolecular amphiphile. Since the ternary complex is stabilized by charge-transfer interaction of an electron donor-acceptor pair inside a host, redox chemistry can be used to trigger the collapse of the vesicles. These novel vesicles may find useful applications in many areas including development of smart materials. We are currently exploring these possibilities.

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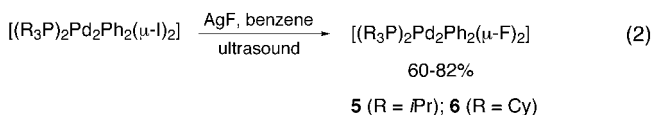
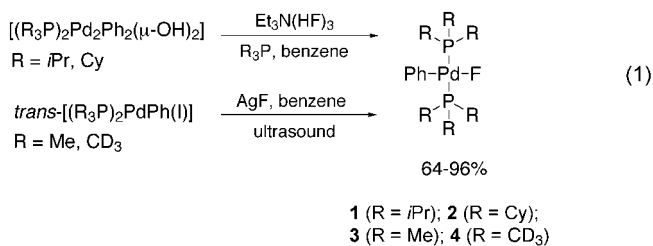
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- [12] The vesicles were prepared as follows: A small amount of THF (0.3–0.5 mL) and distilled water (10 mL) were added to a vial containing an equimolar ratio (6.9  $\mu\text{mol}$ ) of three components: CB[8], viologen with a long alkyl chain ( $\text{C}_{12}\text{VC}_{12}^{2+}$  or  $\text{C}_{16}\text{VC}_{16}^{2+}$ ), and 2,6-dihydroxynaphthalene. The resulting suspension was sonicated at 60°C for 1 h to remove the initially added THF and then kept overnight at room temperature to give a transparent (**2**) or turbid (**3**) solution. The formation of 1:1:1 ternary complexes in **2** and **3** has been confirmed by UV/Vis and  $^1\text{H}$  NMR spectroscopy as well as ESI mass spectrometry. **2**:  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ , 25°C, TMS)  $\delta$  = 8.81 (2H, brs), 8.54 (2H, brs), 7.73 (2H, brs), 7.25 (2H, brs), 6.87 (3H, brs), 6.64 (3H, brs), 6.45 (2H, brs), 5.89 (2H, brs), 5.75 (16H, d), 5.47 (16H, s), 4.54 (3H, s), 4.17 (16H, d), 2.26 (2H, brs), 1.75–1.15 (18H, brs), 0.86 (3H, brs); UV/Vis ( $\text{H}_2\text{O}$ ):  $\lambda_{\text{CT}}$  = 552 nm; ESI-MS:  $m/z$  (%): 914.30 (100) [ $M^{2+}$ ]. **3**:  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ , 25°C, TMS)  $\delta$  = 9.02 (2H, brs), 8.49 (2H, brs), 7.56 (2H, brs), 7.21 (2H, brs), 7.10–6.04 (6H, brs), 5.74 (16H, d), 5.46 (16H, s), 4.16 (16H, d), 2.42–0.65 (34H, brs); UV/Vis ( $\text{H}_2\text{O}$ ):  $\lambda_{\text{CT}}$  = 548 nm; ESI-MS:  $m/z$  (%): 942.86 (70) [ $M^{2+}$ ].
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## Is Fluoride Bonded to Two Pd Acceptors Still Basic? Three $\text{CH}_2\text{Cl}_2$ Molecules Encapsulating a $\text{Pd}_2(\mu\text{-F})_2$ Square and New Implications for Catalysis\*\*

Vladimir V. Grushin\* and William J. Marshall

Organotransition-metal fluoro complexes have recently received much attention due to their useful, uncommon properties,<sup>[1]</sup> and potential use in the synthesis of highly desired, selectively fluorinated organic molecules,<sup>[2–4]</sup> in catalysis,<sup>[5,6]</sup> and in C–H activation.<sup>[7]</sup> Further progress in this new, promising area will depend on firm knowledge of the nature and reactivity of the metal–fluorine bond. As a ligand for the catalytically important platinum group metals, fluoride still remains scantily explored. Thus, being ubiquitous in catalysis, palladium has been shown<sup>[6,8]</sup> to form isolable fluoro complexes only recently. Here we report on the synthesis, unexpectedly strong basicity, and peculiar reactivity of the first dinuclear organopalladium  $\mu$ -fluorides and their mononuclear analogues stabilized by  $(\text{alkyl})_3\text{P}$  ligands.

Using our previously developed methods<sup>[6,8]</sup> we prepared a series of new Pd fluorides **1–6** [Eq. (1) and (2)], which were characterized by analytical, spectroscopic, and X-ray diffraction data (see Supporting Information for details).<sup>[9]</sup>



Considering the particularly strong  $\pi$  basicity of coordinated terminal fluoride<sup>[1,6,10–12]</sup> and the enhanced donating properties of *i*Pr<sub>3</sub>P (compared to Ph<sub>3</sub>P), Pd–F  $d_{\pi}$ – $p_{\pi}$  filled/filled repulsions in **1** and **3** were expected to be stronger than in their Ph<sub>3</sub>P analogue  $[(\text{Ph}_3\text{P})_2\text{PdPh}(\text{F})]$ ,<sup>[8]</sup> resulting in elongation rather than shortening of the Pd–F bond. Surprisingly, the Pd–F bond lengths in both **1** (Figure 1; 2.050(2) and 2.057(2) Å for two structurally similar molecules in the asymmetric unit), and **3** (Figure 2; 2.057(2) Å) are shorter

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