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学 位 論 文 題 目　　両親媒性ピンサー型パラジウム錯体から成るベシクル触媒
　　　　　　　　　　の創製と水中有機分子変換反応への応用

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The self-assembling construction of potentially functionalized, highly-ordered molecular architectures *via* non-covalent interactions among the monomer units is rapidly generating interest from a wide range of chemists. In particular, it has been reported that organic molecules having rigid planar backbones with both hydrophobic and hydrophilic side chains often form bilayer assemblages. If hydrophobic and hydrophilic side chains are incorporated onto the planar NCN palladium pincer backbone, the amphiphilic palladium pincer complexes would adopt a self-assembled architecture having catalytic activity. The author reports the design, preparation, and self-assembling vesicle formation of amphiphilic palladium pincer complexes and their application to the C-C bond forming reactions in water.

The pincer palladium complexes **1** and **2** having pairs of hydrophobic dodecyl chains and hydrophilic tri(ethylene glycol) (TEG) chains, located opposite to one another on the rigid planar
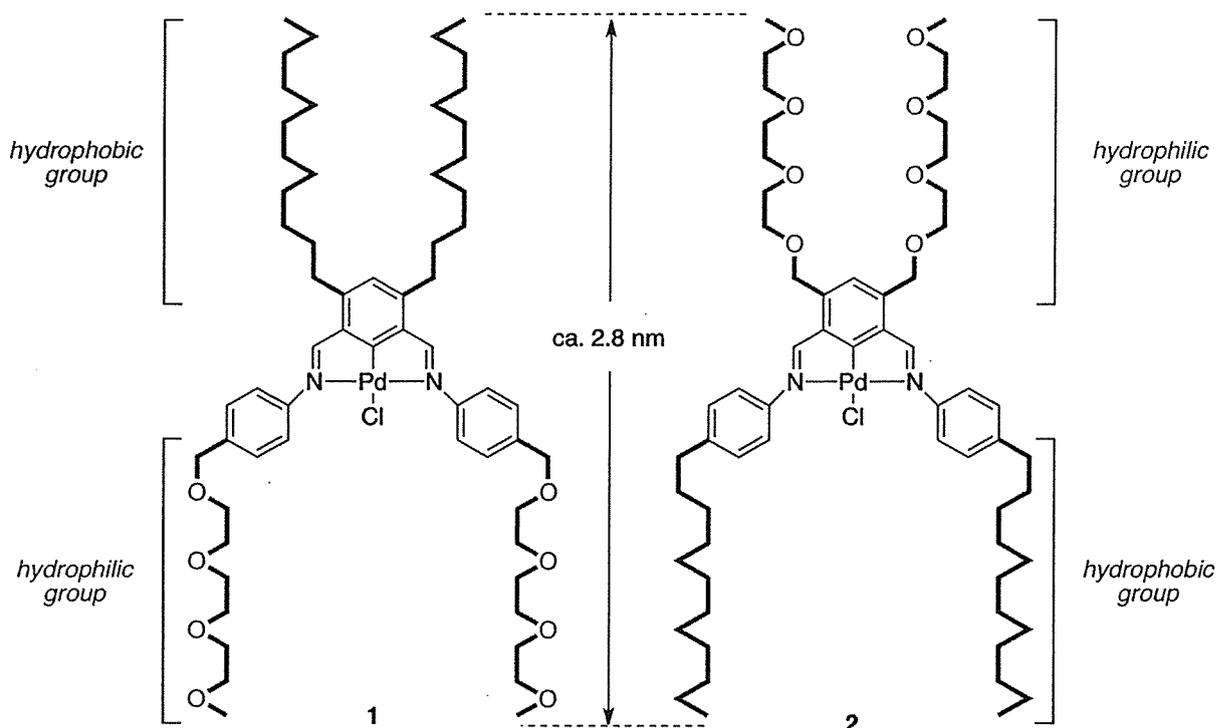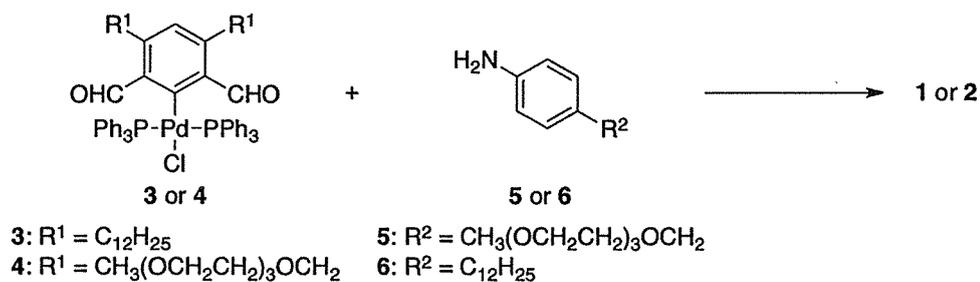
Figure 1. Amphiphilic pincer palladium complexes **1** and **2**

3: $R^1 = C_{12}H_{25}$
4: $R^1 = CH_3(OCH_2CH_2)_3OCH_2$

5: $R^2 = CH_3(OCH_2CH_2)_3OCH_2$
6: $R^2 = C_{12}H_{25}$

Scheme 1. Preparation of amphiphilic pincer palladium complexes **1** and **2**

backbone, were designed for use in the self-assembly formation of vesicles exhibiting catalytic activity in water (Figure 1). These amphiphilic pincer palladium complexes were prepared from their 2,6-diformyl precursors **3** and **4** and primary anilines **5** and **6**, respectively, *via* the ligand introduction route which was previously developed by Uozumi and co-workers (Scheme 1).

With the amphiphilic pincer palladium complexes **1** and **2** in hand, the author next turned his attention to demonstrating their self-assembling potential. After thorough screening, the author was pleased to find that both complexes **1** and **2** exhibited good assembling potential under aqueous conditions. The amphiphilic pincer complex **1** was treated in water at 60 °C for 4 h, and the resulting aqueous mixture was cooled to ambient temperature and vortexed to afford an aqueous slurry of **1**$_{vscl}$. A dynamic light scattering (DLS) study of the slurry demonstrated the formation of the vesicle **1**$_{vscl}$ (average diameter of 550 nm). To an acetonitrile solution of **2** was added water ($H_2O/CH_3CN = 9/1$) and the resulting aqueous mixture was concentrated at 80 °C for 6 h, during which time acetonitrile was slowly vaporized, to afford a pale yellow aqueous suspension. The resulting suspension was cooled and centrifuged (4000 rpm, 15 min) to give precipitates. The precipitates were suspended in water and studied by DLS to demonstrate that the vesicle **2**$_{vscl}$ having an average diameter of 463 nm was formed.

In order to determine the morphologies of bilayer vesicles of **1**$_{vscl}$ and **2**$_{vscl}$, the author performed atomic force microscopy (AFM), scanning electron microscopy (SEM), transmission electron microscopy (TEM) analyses. AFM and SEM analyses revealed the spherical morphologies of **1**$_{vscl}$ and **2**$_{vscl}$ [figure 2(a) and (b) and Figure 3(a) and (b), respectively]. TEM observation of vesicular composites **1**$_{vscl}$ and **2**$_{vscl}$ showed that these composites were hollow structures and the thicknesses of both the vesicle membranes were observed to be ca. 6–7 nm [Figure 4(a) and (b)]. These data are consistent with those of the bilayer membranous structures of **1** and **2** each having both monomer lengths of ca. 2.8 nm in their structures.
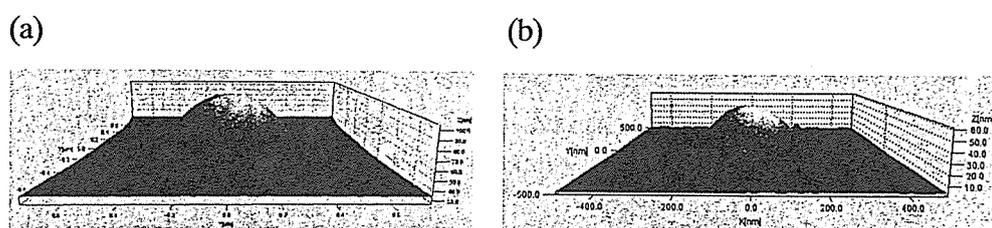
(a)   (b)

Figure 2. AFM images of (a) **1** and (b) **2**

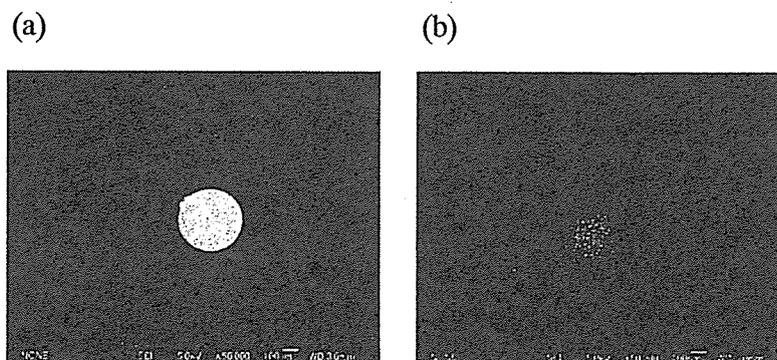(a)   (b)

Figure 3. SEM images of (a) **1** and (b) **2**

(a)   (b)
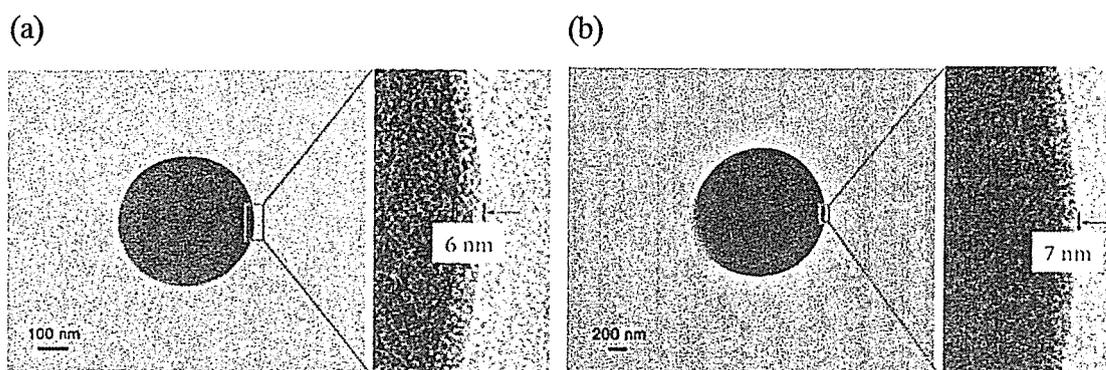

Figure 4. TEM images of (a) **1** and (b) **2**

The incorporation of the fluorescent reagent, fluorescein, into 1_{vscl} revealed a hollow structure with an inner hydrophobic region in the membrane. Thus, when the isolated 1_{vscl} was exposed to fluorescein under aqueous conditions, the fluorescent vesicles, 1_{vscl}/fluorescein, were obtained [Figure 5(a) and Figure 6(a)]. A similar hollow structure of 2_{vscl} was also observed microscopically with the same fluorescence reagent [Figure 5(b) and Figure 6(b)].
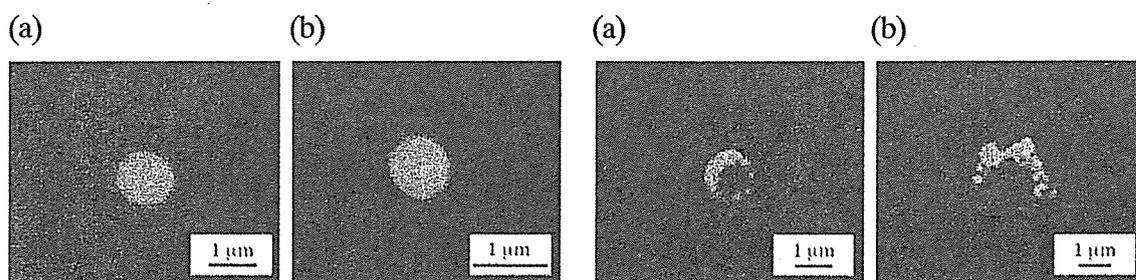
(a)   (b)   (a)   (b)

Figure 5. Fluorescent microscopy images of (a) 1/fluorescein and (b) 2/fluorescein

Figure 6. CLSM images of (a) 1/fluorescein and (b) 2/fluorescein

These experiments demonstrated that the structure of the vesicle 1_{vscl} was similar to that of 2_{vscl}. Therefore, the inversion of the positions of hydrophobic and hydrophilic groups on the pincer backbone did not strongly influence vesicle formation *via* self-assembly of **1** and **2**.

The author next estimated the detailed membranous structure of the vesicle 1_{vscl} using molecular dynamics simulation. Initial molecular structure of the complex **1** was determined by *ab initio* calculation. The molecular dynamics simulation of the bilayer membranous structure of the vesicle 1_{vscl}, which was constructed by 128 molecules of the complex **1** in a basic cell, was carried out in the NPT ensemble at 298.15 K under 1 atm (figure 7). This simulation also supported the formation of the bilayer
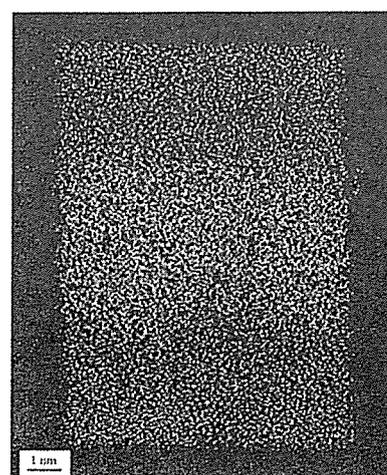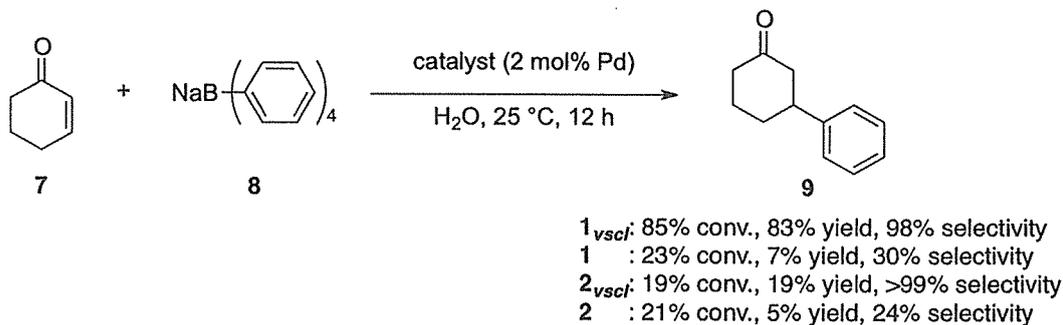

Figure 7. The calculated structure of bilayer membrane of 1_{vscl}

membranous structure. The thickness of the calculated membrane was ca. 6.2 nm and was in good agreement with the observed thickness in TEM analysis.

With the desired vesicles 1_{vscl} and 2_{vscl} in hand, the author next explored their catalytic potential for the Miyaura–Michael reaction of 2-cyclohexene-1-one (7) with sodium tetraphenylborate (8). Significant acceleration of the Miyaura–Michael reaction in water was observed by the formation of vesicles. Thus, the vesicle 1_{vscl} (2 mol% Pd) promoted the Miyaura–Michael reaction of 7 with 8 in water to give the desired arylated product 9 in 83% yield in 12 h with 98% reaction selectivity. In contrast, only a 7% yield of the arylated product 9 was obtained when monomer 1 was used as the catalyst. The reaction of 7 with 8 proceeded in the presence of vesicle 2_{vscl} to provide 9 in 19% yield with >99% reaction selectivity, whereas monomer 2 afforded only a 5% yield of 9 with much lower selectivity. Thus, only slight promotion of the Miyaura-Michael reaction in water was observed by the self-assembling of 2. These results revealed that the construction of self-assembled vesicles is required for the efficient catalysis of the Miyaura–Michael reaction in water. In addition, the catalytic activity of the vesicle 1_{vscl} bearing hydrophilic tri(ethylene glycol) chains close to the palladium center is higher than that of the vesicle 2_{vscl} bearing hydrophobic dodecyl chains close to the palladium center.

1_{vscl}: 85% conv., 83% yield, 98% selectivity
1   : 23% conv., 7% yield, 30% selectivity
2_{vscl}: 19% conv., 19% yield, >99% selectivity
2   : 21% conv., 5% yield, 24% selectivity

Scheme 2. Miyaura-Michael reaction of 2-Cyclohexene-1-one (7) with sodium tetraphenyl borate (8)

The vesicle 1_{vscl} was also effective for the arylating oxirane ring opening reaction of vinyl epoxide 10 with phenylboronic acid (11) to give an 84% yield of the arylated product 12 along with its regioisomer 13 (Scheme 3). However, under similar reaction conditions, the reaction with the monomer 1 did not proceed as efficiently.

1_{vscl}: 84% yield (12/13 = 52/48)
1   : 7% yield (12/13 = 55/45)
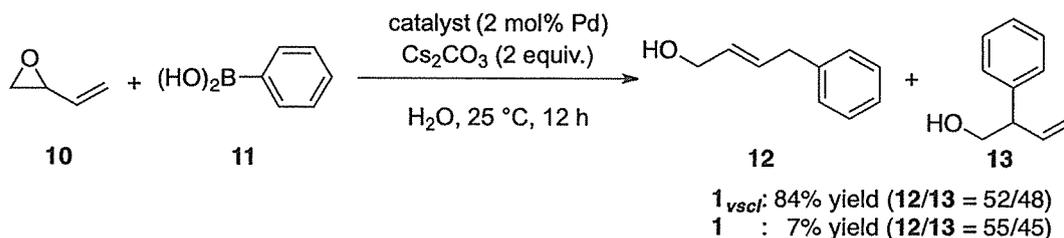
Scheme 3. Palladium-catalyzed oxirane ring opening with PhB(OH)₂

In summary, the author has designed and prepared two amphiphilic pincer palladium complexes bearing hydrophobic or hydrophilic side chains. The prepared complexes were self-assembled in aqueous media to provide bilayer vesicles which were characterized by DLS, various microscopic techniques, and theoretical calculation. The catalytic performances of the obtained

vesicles 1_{vscl} and 2_{vscl} are superior to that of the monomeric complexes **1** and **2** for the Miyaura–Michael reaction in water. In addition, the catalytic activity of the vesicle 1_{vscl} is much higher than that of the vesicle 2_{vscl}. The similar enhancement of the catalytic performance of the vesicle 1_{vscl} was also observed in the arylating oxirane ring opening reaction in water.

博士論文の審査結果の要旨

本論文は序論，本論，結語より構成され，本論は３章から成っている。本論文の眼目は，単分子では触媒低活性あるいは触媒不活性な小分子が自己集積化をへて高次構造体を形成することで初めて触媒活性を獲得するという新しい触媒反応駆動システムの提案にあり，とくに水中での有機分子変換触媒システムの駆動に着目している。序章では従来の水中触媒機能発現例とその原理，また水中での小分子自己集積化による高次構造体形成の先例と原理，それら高次構造体が触媒活性を呈する先例，本論文で開発するピンサー型錯体構造に着想を得た背景，などが簡潔に紹介されている。

本論１章では，標的とする２つのピンサー錯体の構造設計の着想，合成戦略，実際の合成，合成した錯体の構造解析について詳細に記述されており，また実験の部には実験法と各種機器データについて十分な記述がある。とくに標的錯体の合成に利用した「リガンド導入法」と称する新しいピンサー型錯体合成経路は出願者所属研究室独自の成果である。

本論２章では前章で得た２種のピンサー錯体の自己集積化による２分子膜ベシクル構造形成について詳細に述べられている。ベシクル形成は動的光散乱，原子間力顕微鏡，走査型電子顕微鏡，透過型電子顕微鏡，蛍光顕微鏡，共焦点レーザー顕微鏡，さらにはSPring8を利用した微小角入射Ｘ線回折などを駆使して徹底的に検討されている。これはこれまでに第一級の国際学術誌に報告されている自己集積構造体の構造研究等と比較しても徹底した検討であり，ベシクル構造の詳細とその外部有機分子取込みに関する基礎知見の獲得に成功している。さらに，ベシクルを形成する２分子膜構造を分子レベルで理解すべく，計算科学的手法によるシミュレーションを行っている。*ab initio*計算によるピンサー錯体構造最適化，同構造を初期座標としCHARMM分子力場ポテンシャルを利用するMD計算を実施し，また２分子膜構造体における錯体密度計算，２分子構造の微細構造シミュレーションなどをソフトとしてMODYLASを利用して実施し，その結果を実験観測結果と照合している。これら結果から２分子膜構造の更なる構造証明，膜内でのピンサー錯体の集積微細構造などが示されている。

本論３章では１，２章で得られたピンサー錯体ベシクル構造体を利用する水中での有機分子変換触媒について論述されている。Miyaura-Michael反応，アリールホウ酸試薬によるオキシラン環のアリール化開環反応が水中で進行し，目的生成物を与えている。ここではベシクル構造形成を伴わないピンサー錯体単分子は触媒活性が顕著に低く，ベシクル構造形成が水中触媒機能発現に本質的に寄与していることが合理的に実証されている。その実験結果について２分子膜構造内部での疎水性領域の形成が鍵であろうことが合理的に考察され，示された実験結果をよく説明している。

すなわち，触媒不活性な小分子が自己集積化をへて疎水性領域を獲得し，疎水性領域への有機基質の能動的拡散によって自発的高濃度反応場が形成され，この反応場には予め潜在的に触媒機能を持ちうる遷移金属が組み込まれていることから，自発濃縮した有機基質は触媒反応に附されることとなる。

このように不活性小分子がまるで知性を持つかのように自らの性質によって活性を獲得し，さらにそこに基質を取込み分子変換を駆動させる全く新しい触媒駆動システムと理解でき，熱や光などの外的エネルギーに依らない反応駆動の可能性を世に示したものとして大いに

評価できる。

以上，学術的到達点は高く，実験内容も充実している。これら成果の一部はすでに2報の査読付き国際学術誌に掲載済みであり語学力も十分なレベルにあると判断される。以上より本論文は博士（理学）の学位授与に値するものと審査委員全員一致で判断した。