

氏 名 櫻井 扶美恵

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学位論文題目 Development of Aquacatalytic Systems Based on the Self-
Assembly of Amphiphilic Pincer Palladium Complexes

論文審査委員 主 査 教授 加藤 晃一
教授 魚住 泰広
准教授 榎山 儀恵
准教授 江 東林
准教授 藤川 茂紀 九州大学

論文内容の要旨
Summary of thesis contents

Construction of bilayer vesicles by self-assembly of amphiphiles has attracted widespread interest in various research areas due to their use as models for biological membranes and their practical applications such as drug delivery, cosmetics, and so on. It has been reported that organic molecules having a rigid planar backbone with both hydrophilic and hydrophobic side chains often formed bilayer architectures. If both hydrophilic and hydrophobic side chains are incorporated onto planar transition metal complexes, the resulting amphiphilic complexes would adopt self-assembled architectures with bilayer membranes having catalytic activity. The use of the self-assembled architectures would achieve effective transformation in water. The author herein reports the development of an aquacatalytic system based on the self-assembly of amphiphilic transition metal complexes.

This thesis is composed of general introduction, main issues (Chapter 1–4), and general conclusion.

In general introduction, the author shows the background on vesicles and their application to catalysis.

In Chapter 1, the synthesis of amphiphilic NNC-pincer palladium complexes is described.

In Chapter 2, the investigation of the catalytic activity of an NNC-pincer palladium complex for the allylic arylation is described.

In Chapter 3, the vesicle formation by the self-assembly of the prepared amphiphilic NNC-pincer palladium complexes in water is described.

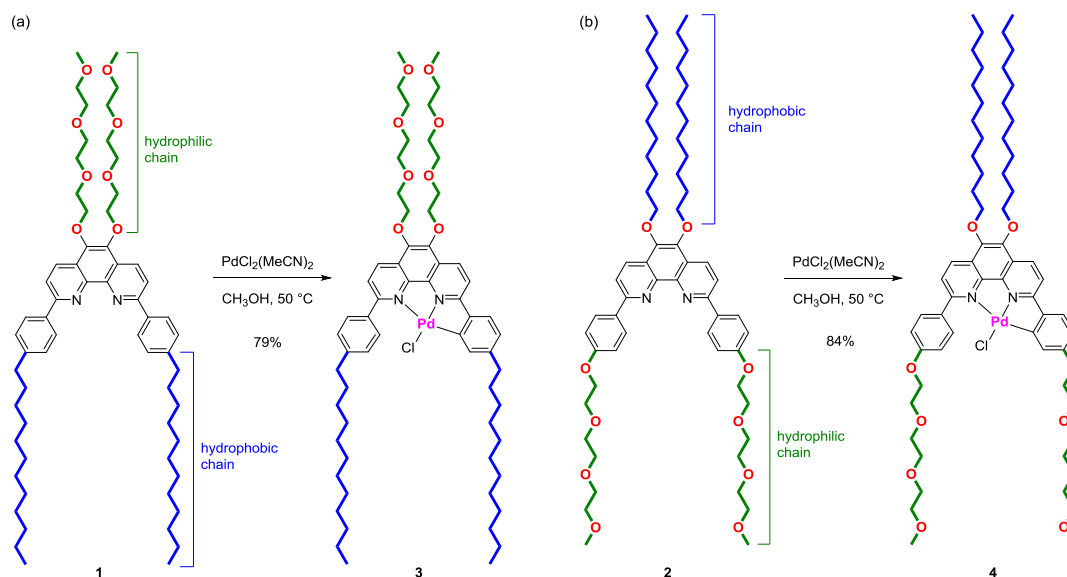
In Chapter 4, the application of the obtained vesicles to the allylic arylation and Cu-free Sonogashira reaction in water is described.

Finally, the author mentions general conclusion of this thesis.

Chapter 1

The author designed amphiphilic phenanthroline ligands **1** and **2** bearing hydrophilic tri(ethylene glycol) (TEG) chains and hydrophobic dodecyl chains. The amphiphilic ligands **1** and **2** were synthesized from 1,10-phenanthroline-5,6-diol in 3 steps. The ligands **1** and **2** underwent the complexation with dichlorobis(acetonitrile)palladium(II) in methanol at 50 °C (Scheme 1). ¹H-NMR, ¹³C-NMR, ESI-TOF mass, and elemental analyses of the products obtained by the complexation revealed the formation of unexpected amphiphilic NNC-pincer palladium complexes **3** and **4**.

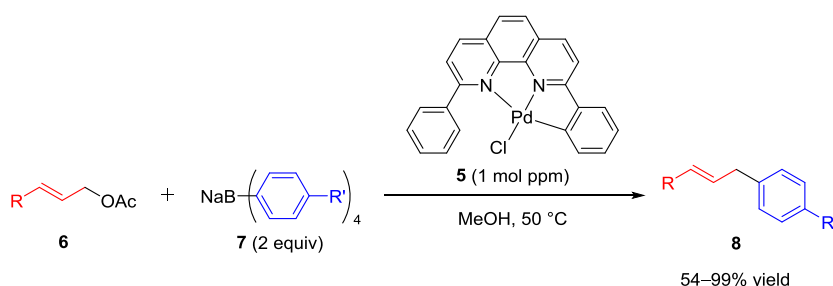
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Scheme 1. Complexation of amphiphilic phenanthroline ligands **1** and **2** with $\text{PdCl}_2(\text{MeCN})_2$.

Chapter 2

To investigate the catalytic activity of an NNC-pincer palladium complex **5**, the complex **5** was applied to the allylic arylation. The reaction of aromatic and aliphatic allyl acetates **6** with sodium tetraarylborates **7** in the presence of 1 mol ppm of the complex **5** in methanol at 50 °C gave the corresponding arylated products **8** in 54–99% yield (Scheme 2). The reaction with 1 mol ppb of the complex **5** also proceeded. The turnover number (TON) and frequency (TOF) of **5** reached up to 500,000,000 and up to 11,250,000 h^{-1} , respectively. The reaction pathway of the allylic arylation was also investigated.



Scheme 2. Allylic arylation of allyl acetates **6** with sodium tetraarylborates **7**.

Chapter 3

The self-assembling behavior of the amphiphilic NNC-pincer palladium complexes **3** and **4** is described. After screening of the self-assembling conditions, the author found that both complexes **3** and **4** self-assembled in water to form vesicles 3_{vscl} and 4_{vscl} . Thus, the complex **3** was heated in water at 60 °C for 4 h without stirring. After slow cooling to 25 °C overnight, the resulting mixture was sonicated for 15 min to afford a yellow suspension. Self-assembling

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experiment of the complex **4** was also examined. The complex **4** was heated in water at 80 °C for 12 h without stirring. The resulting aqueous mixture was cooled to 25 °C and then sonicated for 10 min, affording a yellow suspension. Dynamic light scattering (DLS) analyses of these suspensions showed that average diameters of the vesicles 3_{vscl} and 4_{vscl} were 554 and 985 nm. In order to determine the morphologies of vesicles 3_{vscl} and 4_{vscl} , the author carried out the characterization with transmission electron microscopy (TEM), atomic force microscopy (AFM), fluorescence microscopy, and confocal laser scanning microscopy (CLSM). TEM and AFM analyses of the vesicles revealed the formation of spherical structures (Figures 1 and 2). TEM analysis also showed the thicknesses of the membranes of the vesicles 3_{vscl} and 4_{vscl} to be 14 and 32 nm, respectively (Figure 1).

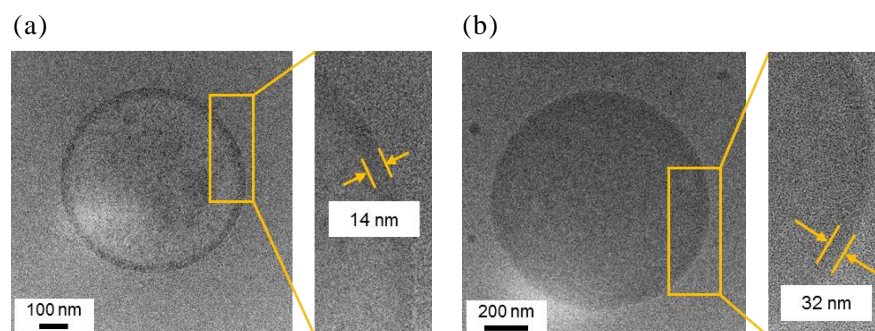


Figure 1. TEM images of 3_{vscl} (a) and 4_{vscl} (b).

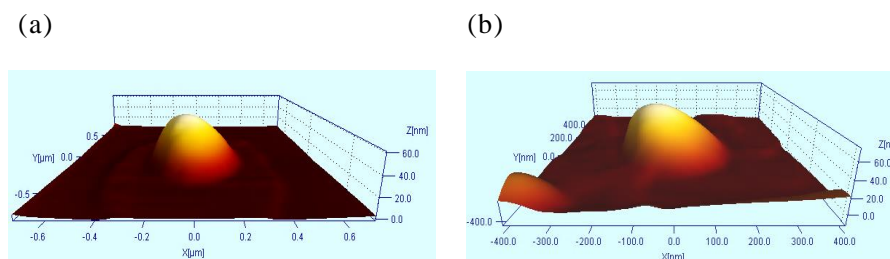


Figure 2. AFM images of 3_{vscl} (a) and 4_{vscl} (b).

The author conducted dyeing experiments with fluorophores to confirm the presence of the membranes of the vesicles 3_{vscl} and 4_{vscl} . The addition of fluorescein as a fluorophore to aqueous suspensions of 3_{vscl} and 4_{vscl} gave fluorescent vesicles 3_{vscl} /fluorescein and 4_{vscl} /fluorescein. Fluorescence microscopic observation of the prepared vesicles (3_{vscl} /fluorescein, 4_{vscl} /fluorescein) showed the existence of a hydrophobic region in the membrane of the vesicles (Figure 3). In addition, CLSM analyses of the fluorescent vesicles revealed that the self-assembled architectures were not micelles or oil droplets but vesicles with an inner hydrophobic region in the membranes (Figure 4).

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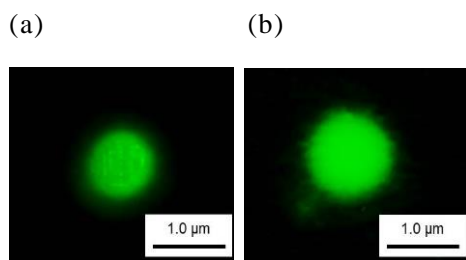


Figure 3. Fluorescent microscopic images of (a) 3_{vscI} /fluorescein and (b)

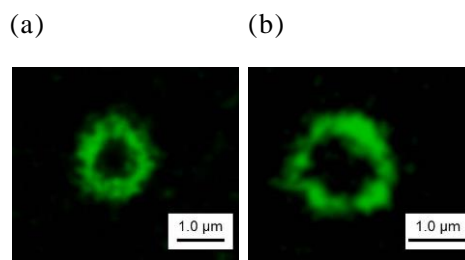
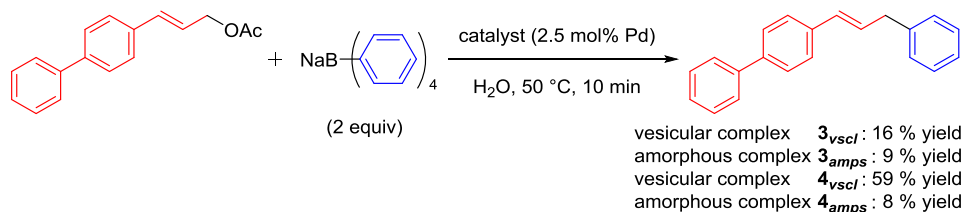


Figure 4. CLSM images of (a) 3_{vscI} /fluorescein and (b) 4_{vscI} /fluorescein.

Chapter 4

The author investigated the catalytic potential of the vesicles 3_{vscI} and 4_{vscI} for the allylic arylation in water. The allylic arylation of (*E*)-3-(4-phenylphenyl)-2-propen-1-ol acetate with sodium tetraphenylborate took place in the presence of the vesicle 3_{vscI} in water at 50 °C for 10 min to give the arylated product in 16% yield (Scheme 3). When the amorphous complex 3_{amps} was used as the catalyst, 9% yield of the product was obtained. The formation of the vesicle 3_{vscI} slightly improved the yield of the arylated product. The vesicle 4_{vscI} also promoted the reaction, affording the product in 59% yield. In contrast, the reaction with the amorphous complex 4_{amps} gave the product in only 8% yield. The reaction was also performed in organic solvents such as 1,2-dichloroethane, toluene, THF, acetonitrile, methanol, and DMF, giving the product in low yield (0–14% yield). The formation of the vesicle 4_{vscI} was shown to be essential to accelerate the reaction. Various allyl acetates and sodium tetraarylborates underwent the reaction with the vesicle 4_{vscI} to afford the corresponding arylated products.

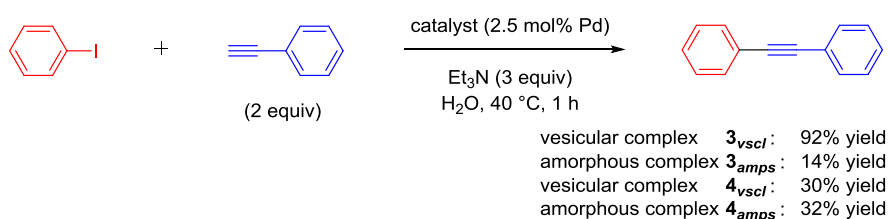


Scheme 3. Allylic arylation of (*E*)-3-(4-phenylphenyl)-2-propen-1-ol acetate with sodium tetraphenylborate.

The catalytic activity of vesicles 3_{vscI} and 4_{vscI} was also examined for the Cu-free Sonogashira coupling reaction in water. The vesicle 3_{vscI} catalyzed the coupling reaction of iodobenzene with phenylacetylene in water at 40 °C for 1 h to give diphenylacetylene in 92% yield. In contrast, only 14% yield of the product was obtained when the amorphous complex 3_{amps} was used in the reaction

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(Scheme 4). The formation of the vesicle 3_{vscI} was required to perform the reaction effectively. The reaction was also conducted in the presence of the vesicle 4_{vscI} and the amorphous complex 4_{amps} , affording diphenylacetylene in 32 and 30% yield, respectively. No acceleration of the reaction by the formation of 4_{vscI} was observed. When dichloromethane, toluene, THF, acetonitrile, and methanol were used as the solvent, the reaction gave only 3–11% yield of the product. The vesicle 3_{vscI} accelerated the reaction of various aryl iodides with alkynes to provide the corresponding internal alkyne products.



Scheme 4. Cu-free Sonogashira coupling of iodobenzene with phenylacetylene.

The results obtained in the allylic arylation and the Cu-free Sonogashira coupling demonstrated that direction of hydrophilic TEG chains and hydrophobic dodecyl chains attached to the phenanthroline backbone influenced the acceleration of the reaction.

Summary of the results of the doctoral thesis screening

本論文は序論、4章から成りたつ本論、結論から構成されている。本論文では、単分子では十分な触媒活性を発揮しない錯体小分子が自己集積化により高次構造体を形成することで触媒活性を獲得するという触媒駆動原理に基づいた新しい触媒反応システムの設計と構築について述べられている。また、ベシクル形成を指向し合成した両親媒性錯体分子の中心構造である錯体分子の触媒活性を評価する中で、ごく少量の触媒量で十分に機能する非常に高い活性を示す分子であることも見出している。

序論では従来のベシクル形成とその原理、ベシクルの水中触媒反応への応用に関する先例、本論文で開発する両親媒性錯体の設計への着想に至る背景、などが簡潔にまとめられている。

第一章では、標的とする2つの両親媒性錯体の構造設計、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。特に、当初の分子設計とは異なるピンサー型錯体が得られていることから、その構造同定へと至った機器解析について詳細に述べられている。

第二章では、第一章にて合成した両親媒性ピンサー型錯体の中心構造の触媒機能を評価している。ピンサー型錯体が酢酸アリル誘導体とテトラアリアルホウ酸ナトリウムの反応を触媒し、対応するアリアル化生成物を良好な収率で与えている。その触媒回転数は最大で5億に達しており、非常に高い活性を示している。基質適用性に関しても詳細に検討が加えられ、反応機構に関しても実験化学的検討を行い、その議論を行っており、十分に錯体分子の触媒機能について議論されている。

第三章では、第一章で得た2種の両親媒性パラジウムピンサー型錯体の自己集積化によるベシクルの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、透過型電子顕微鏡、蛍光顕微鏡、共焦点走査型顕微鏡を駆使して確認されている。また、共焦点走査型顕微鏡による観察結果からは、外部有機分子取り込みに関する基礎的な知見を得ている。

第四章では、前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反応について論述されている。アリル位アリアル化反応、銅非存在下でのSonogashira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に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ベシクルを構成している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。

結論では論文全体を総括している。

以上のように、本論文では、両親媒性パラジウムピンサー型錯体の合成、その中心骨格の触媒活性評価、両親媒性ピンサー型錯体の自己組織化によるベシクル構造体の構築、そして、得られたベシクル構造体を触媒とした水中有機分子変換反応を報告している。本論

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文の学術到達度は高く、実験内容も充実している。本論文の成果一部は、既に3報の査読付き国際学術誌に発表されており、その内容は国際的にも高い水準であると評価された。

以上により、本論文は博士(理学)の学位授与に値するものと審査員全員一致で判断した。