

# 論文の内容の要旨

## Well Designed, Heterogeneous Gold, Palladium, and Rhodium Nanoparticles as Catalysts for Organic Transformations (精密に設計された不均一系金、パラジウム、 及びロジウムナノ粒子触媒の開発と その有機合成への応用)

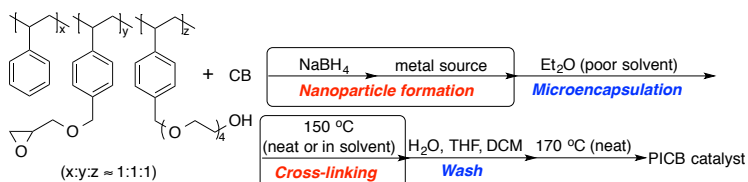
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### 1. Introduction

Metal nanoclusters (NCs) and nanoparticles (NPs) have been widely used as heterogeneous catalysts due to their distinct characteristics, which differ from both bulk metals and metal complexes resulted from their increased surface area and quantum size effect, and recently, many examples have been reported about organic synthesis catalyzed by metal NPs. The catalytic activity/selectivity of metal NCs/NPs are affected by various factors, but many of them are still veiled and knowledge about how they work on metal NP catalysis is insufficient.

In our laboratory, we have developed polymer incarcerated metal NP catalysts (PI catalysts) for organic transformations by immobilization of metal NPs using polystyrene-based copolymer through microencapsulation and cross-linking steps (Scheme 1).<sup>[1]</sup> In this catalyst, metal NPs are stabilized by multiple weak interaction of  $\pi$ -

Scheme 1. Preparation method of PICB catalyst



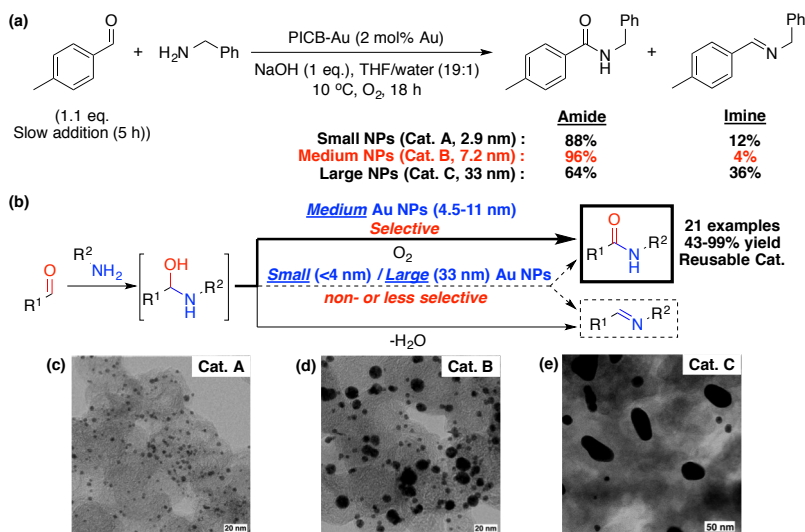
electron of benzene ring. This weak but multiple interactions between polymer support and metal NPs provide not only high activity of metal NPs but tunability of size of metal NPs. Another important advantage of using polymeric supports is their easy modification. Diverse catalytic systems can be constructed by structure change of monomer/polymer and introducing specific functional groups. In my Ph.D researches, I tried to develop well designed, heterogeneous metal NP catalysts for organic transformations. As a result, it was confirmed that activity and selectivity of metal NPs were controllable by changing their sizes or existence of ligands in polymer supports. Very rare size effect and characteristic ligand immobilization effect were also found.

### 2. Results and Discussion

#### 2.1 Size effect of Au NPs in direct amide synthesis through aerobic oxidation from aldehydes

Size of metal NCs/NPs is one of the important factors to determine their activity. In the case of NCs, there is optimal size for each reaction. On the other hand, it is generally accepted that smaller NPs have higher activity than larger ones because of their increased surface area and reverse examples are very rare. Previously in our laboratory, successful results were obtained for selective amide synthesis through tandem oxidation process (TOP) with PICB-Au or PICB-Au/Co catalysts<sup>[2]</sup> and imine synthesis with PICB-Au/Pd catalysts from alcohols and amines.<sup>[3]</sup> Based on these results, I investigated direct amide synthesis through aerobic oxidation from aldehydes and amines using various Au NP catalysts of different size.

## Scheme 2. Aerobic oxidative amidation from aldehydes and amines

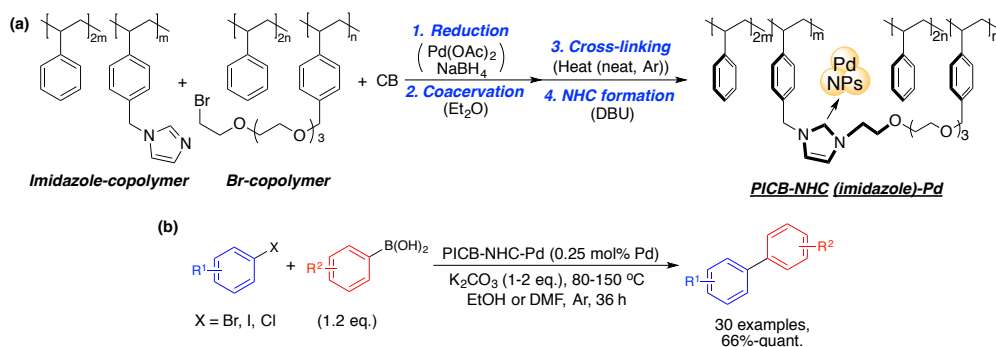


large sizes (Cat C, Scheme 2-(e)), amide selectivity was not satisfactory. Surprisingly, when Au NPs of medium size (Cat. B, Scheme 2-(d)) were used, selectivity toward an amide product was increased and a high yield of the amide product was obtained. As a result, correlation between size of Au NPs and amide selectivity was observed regardless of their preparation method. This is very rare example of high activity and selectivity with Au NPs of medium size. This reaction system showed broad substrate generality and catalysts could be recovered and reused several times without significant decrease of their activities (Scheme 2-(b)). Also, in the reactions from benzylic alcohols and primary amines, through 2 steps of oxidation reaction, good results were obtained. Probably, two factors would be important to determine the selectivity toward amide; the interaction between Au NPs and amines/amides (adsorption and desorption), and oxidation ability of metal NPs. Both were changed by the size of Au NPs, and it was concluded that balance between these two factors was featly good in Au NPs of medium size for the selective amide formation.

## 2.2. Immobilized ligand (NHC) in Suzuki-Miyaura coupling reaction

Pd NPs have been widely used as powerful catalysts in various kinds of reactions, and in some cases, their activities and selectivities are improved in the presence of ligands. To develop more efficient catalytic system, immobilization of both ligands and Pd NPs is a good way but design of stable structure of catalysts is still challenging. Previously, our laboratory reported Ni NP catalysts immobilized by polymer containing *N*-heterocyclic carbene (NHC), and it showed excellent activity and robustness in Corriu-Kumada-Tamao coupling reaction.<sup>[4]</sup> I thought that Pd NP catalysts using NHC-containing polymer could be synthesized and they would give different activity or selectivity compared with that of Pd NP catalysts, which did not contain an NHC ligand.

### Scheme 3. Preparation of PICB-NHC-Pd and its use in Suzuki-Miyaura reaction



PICB-NHC-Pd catalyst was prepared with two different copolymer moieties, imidazole-containing copolymer and Br-containing copolymer as shown in Scheme 3-(a). In this catalyst, NHC has dual roles as a ligand and a cross-linker. Generation of NHC was confirmed

by SR-MAS NMR analysis and the result of STEM/EDS analysis showed formation of Pd NPs. This PICB-NHC-Pd catalyst showed excellent activity in Suzuki-Miyaura coupling reaction of aryl bromide and iodide. In the case of aryl chloride, also excellent results were obtained although harsher conditions were needed compared with that of aryl bromide and iodide. Under optimized reaction conditions, low yield of desired product was obtained with small amount of Pd leaching when PICB-Pd catalyst which does not containing NHC moiety was used instead of PICB-NHC-Pd. Even with external addition of NHC ligands, further decreased yield was observed with Pd

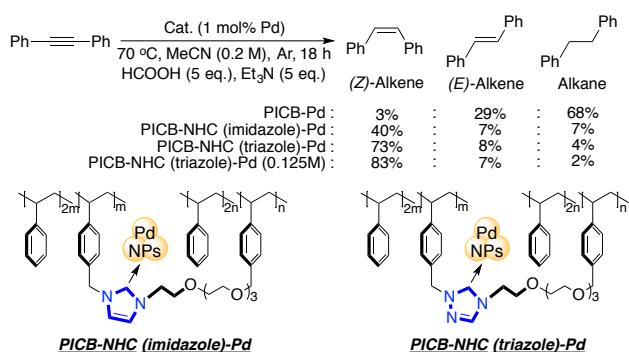
leaching, therefore, the good effect of incorporated NHC was confirmed for promoting the activity of Pd NPs and stabilizing them. Also, synergistic effect was observed by immobilization of an NHC ligand compared with their external addition. In the case of recovery/reuse of the catalyst, it could be reused several times maintaining its activity after simple wash with a slightly basic solution (Scheme 3-(b)).

### 2.3. NHC moiety immobilized with Pd NPs in transfer semi-hydrogenation

Use of ligands in metal NP catalytic systems could make them have higher activity as shown in Suzuki-Miyaura coupling reaction with PICB-NHC-Pd catalyst, but it is also widely accepted that selectivities (chemo-, region-, diastereo-, etc.) could also be tuned by existence of ligands.

Transfer semi-hydrogenation using triethylammonium formate as a hydrogen source is a good way for selective (*Z*)-alkene formation because of precise control of the amount of hydrogen source, and it can prevent over-hydrogenation or isomerization. With diphenylacetylene as a substrate, transfer semi-hydrogenation was investigated using different catalytic systems, and as a result, immobilized NHC effect was observed (Scheme 4); In the case of PICB-Pd catalyst, it gave alkane as a major product. However, (*Z*)-alkene selectivity was increased with imidazole NHC moiety incorporated catalyst, and further increased (*Z*)-alkene selectivity and yield were obtained with triazole NHC immobilized catalyst. Also, concentration of reaction system affected to yield and selectivity toward (*Z*)-alkene. As a result, it was found that the activity and selectivity were changed by choice of immobilized NHC structures, and in our hypothesis, NHC has a deactivation effect on Pd NPs to educe selectivity toward (*Z*)-alkene formation.

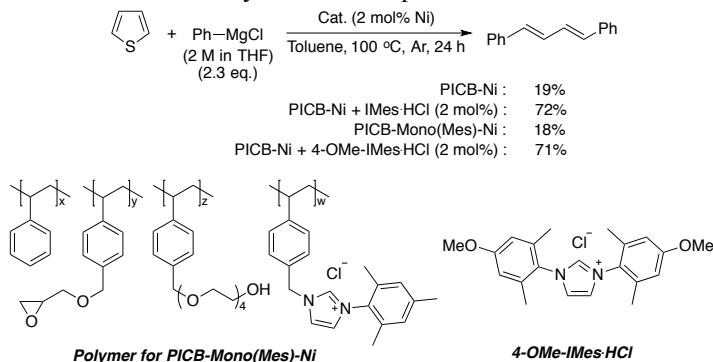
**Scheme 4.** Transfer semi-hydrogenation with Pd NP catalysts



### 2.4. NHC effect in Wenkert arylation of thiophene

Wenkert arylation of thiophene catalyzed by Ni catalyst is one of the useful reaction for synthesis of 1,4-diaryl-1,3-butadiene but there is no example using heterogeneous catalyst. Previously reported PICB-NHC-Ni catalyst was tried for this reaction, but very low yield of desired product was observed, therefore, new catalyst design was tried (Scheme 5). In the presence of externally added IMesHCl with PICB-Ni catalyst, high yield of desired product was obtained, but with PICB-NHC (Mono-Mes)-Ni catalyst, no improvement was observed compared with the result of PICB-Ni, probably due to the lack of steric bulkiness. With 4-OMe-IMesHCl, high yield was obtained, and this moiety is thought as proper group for incorporation in polymer structure.

**Scheme 5.** Wenkert arylation of thiophene with Ni NPs and NHCs

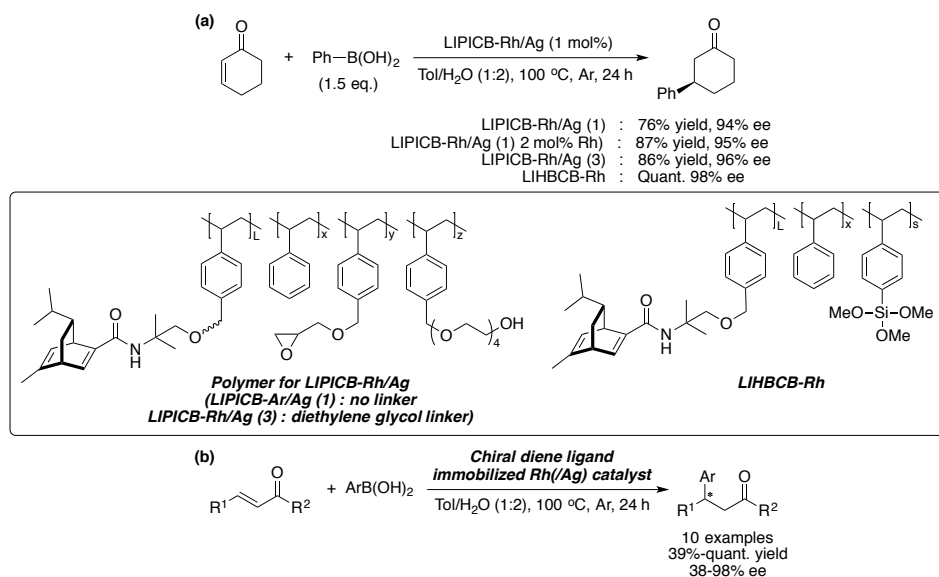


### 2.5. Development of chiral diene immobilized Rh NPs in asymmetric 1,4-addition of boronic acid

There is almost no example about immobilization of chiral ligand with metal NP catalyst that shows high enantioselectivity, and development of this kind of heterogeneous catalyst is important task. Our laboratory reported asymmetric 1,4-addition of boronic acid to  $\alpha,\beta$ -unsaturated carbonyl compound catalyzed by Rh/Ag nanoparticle catalyst (PICB-Rh/Ag) in the presence of amide substituted chiral diene ligand.<sup>[5]</sup> This catalytic system showed high yield and ee, and PICB-Rh/Ag catalyst can be successfully recovered and reused several times. However, precious amide substituted chiral diene ligand should be externally added in every reaction; if immobilization of chiral diene with Rh nanoparticle, simpler and more efficient catalytic system would be realized such as recovery and reuse of both ligand and Rh nanoparticle is possible. Various types of ligand immobilized monomers, polymers and Rh nanoparticle catalysts were synthesized with different linkers and cross-linking moieties; In the case of LIPICB-Rh/Ag catalysts, in which epoxy monomer and alcohol monomer were used as cross-linkers, different linkers were tried and it was found

that hydrophilicity and length of linker are important for activity of this catalyst in asymmetric 1,4-addition of boronic acid to cyclic enone (Scheme 6-(a)). Cross-linking temperature was also one of the important factors to affect catalytic activity due to decomposition of chiral diene moiety under high temperature. Organic-inorganic hybrid catalyst, in which trimethoxysilyl moiety was used as cross-linking moiety, were also prepared and chiral diene ligand was successfully immobilized with Rh nanoparticle. This LIHBCB-Rh catalyst showed higher yield and ee compared with the result with LIPICB-Rh/Ag catalyst and it provides the possibility for further development of chiral ligand immobilized Rh nanoparticle catalyst which has high activity in terms of both yield and enantioselectivity (Scheme 6-(a)). With these chiral ligand immobilized Rh nanoparticle catalysts, substrate scope in asymmetric 1,4-addition of boronic acids to enones were also conducted and moderate to excellent results were obtained (Scheme 6-(b)). In addition, coating of Rh/cellulose catalyst with chiral diene ligand immobilized polymer was also possible and it showed excellent enantioselectivity although yield was low; it suggested new approach for incorporation of chiral ligand though further investigation would be needed.

**Scheme 6.** Asymmetric 1,4-addition of boronic acid catalyzed by chiral ligand immobilized Rh NP catalysts



### 3. Conclusion

During my Ph.D studies, I found important effects to control activity and selectivity of metal NP catalysts; size of metal NPs and immobilization of ligand (NHC, chiral diene). Activity/selectivity of metal NPs was highly dependent on these factors. These polymer-incarcerated metal NP catalysts showed excellent activity and robustness in redox reactions and cross-coupling reactions. This research has provided valuable knowledge about the activity/selectivity of heterogeneous metal NP catalysts and how they work on. I believe that these results may contribute to find out a new possibility and a strategy for designing metal NP catalysts in the field of heterogeneous catalysis and organic synthesis.

### 4. References

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