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学位論文題目 Development of Green-Sustainable Copper Catalysts
Immobilized on Polystyrene-Based Resins to Achieve
Efficient Organic Transformations

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論文内容の要旨
Summary of thesis contents

Development of highly efficient organic molecular transforming systems using transition-metal catalysts has been widely recognized as one of major challenges in modern organic chemistry. In particular, the social demand to realize green-sustainable society has recently promoted chemists to develop green-sustainable organic transformations with transition-metal catalysts for the synthesis of various organic compounds including natural products, medicine, functional organic materials, and so on. In conventional organic transformations with the transition-metal catalysts, precious metals such as Pd, Pt, Rh, and so on which are expensive and limited on earth have been utilized. The most reactions have been conducted under homogeneous conditions. In order to realize high green-sustainability in the organic transformations, it is desirable to recycle the catalysts and replace the limited precious metal species with ubiquitous metal species such as Cu, Fe, and so on which are cheap and abundant on earth.

Heterogeneous switching of homogenous transition-metal catalysis has been attracted much attention as one of the key strategies to achieve the high green-sustainability and provides considerable advantages in terms of the recovery and reuse of the catalysts and the reduction of metal contamination of the resulting products. Uozumi and co-workers have contributed to this research field and so far developed a variety of transition-metal catalysts immobilized on polystyrene-based resin-supports to realize various organic transformations with high efficiency. However, most immobilized transition-metal catalysts require expensive precious transition-metals (such as Pd, Pt, Rh, and Ir), and the use of cheaper ubiquitous transition-metals such as Cu or Fe in the immobilized catalysts is yet immature. With regard to improving the green-sustainability in organic transformations, the development of immobilized catalysts containing ubiquitous transition-metals is highly desirable. In this thesis, the author developed new heterogeneous copper catalysts immobilized polystyrene-based resins which efficiently catalyzed the oxidative homocoupling reaction of terminal alkynes, the Huisgen 1,3-dipolar cycloaddition reaction, and the aerobic oxidation of alcohols with high recyclability.

This thesis consists of General introduction, Main subjects (Chapters 1-3), and General conclusion.

In **General Introduction**, the author mentions the background for the heterogeneous catalysts.

In **Chapter 1**, the author describes development of recyclable polystyrene (PS)-supported copper(II) *N,N,N',N'*-tetraethyldiethylenetriamine catalysts for the aerobic oxidative homocoupling of terminal alkynes.

In **Chapter 2**, the author describes development of polystyrene-poly(ethylene glycol) resin (PS-PEG)-supported copper(II)-triazine-based dendrimer catalyst

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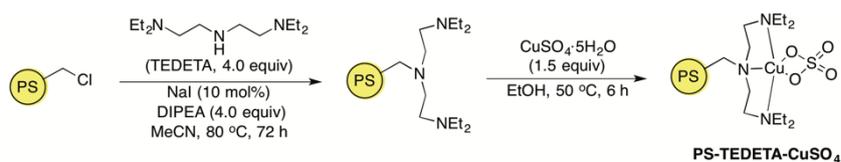
(CuSO₄-TD_{2.0}@PS-PEG) and the application to the Huisgen 1,3-dipolar cycloaddition in water.

In **Chapter 3**, the author describes the further application of PS-PEG-supported copper(II)-triazine-based dendrimer catalyst [Cu(OAc)₂-TD_{2.0}@PS-PEG] to the aerobic oxidation of alcohols.

In **General Conclusion**, the author summarizes the work of the thesis.

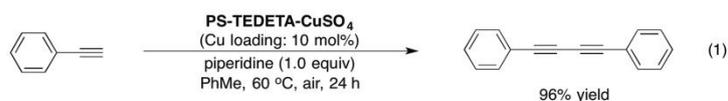
Chapter 1

The author developed recyclable polystyrene-supported copper(II) *N,N,N',N'*-tetraethyldiethylenetriamine [Cu(II)-TEDETA] complexes for the aerobic oxidative homocoupling of terminal alkynes. The polystyrene-supported Cu(II)-TEDETA complexes were prepared by immobilization of *N,N,N',N'*-tetraethyldiethylenetriamine (TEDETA) onto crosslinked polystyrene, followed by complexation of copper salts (Scheme 1). The immobilized TEDETA and copper-TEDETA catalysts were characterized by SR/MAS NMR, FT-IR spectroscopies and ICP-AES.



Scheme 1. Preparation of PS-TEDETA-CuSO₄

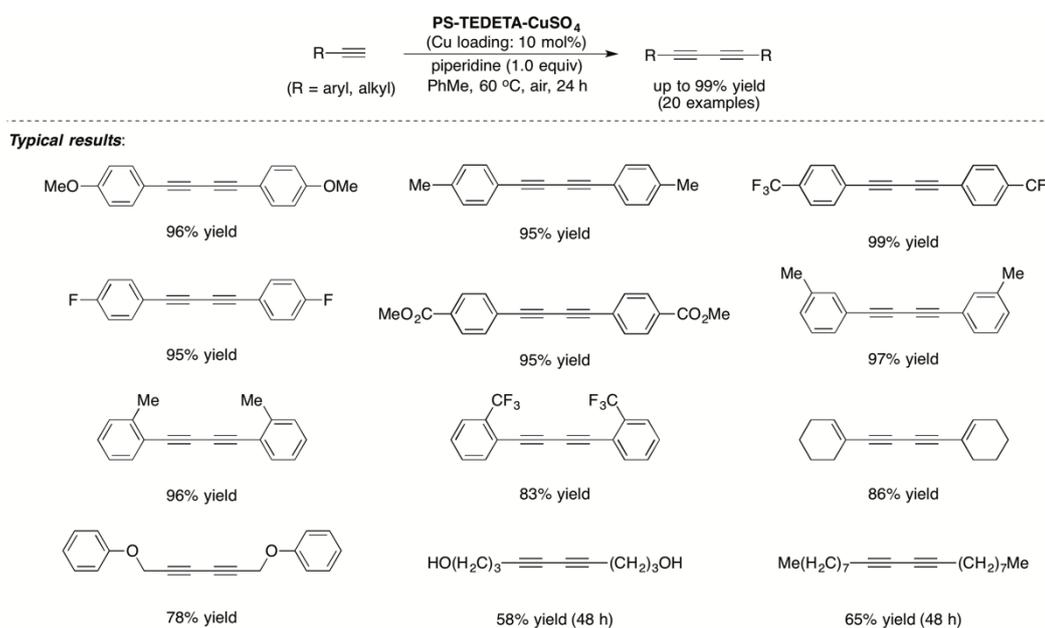
When the polystyrene-immobilized CuSO₄-TEDETA catalyst was applied to the oxidative homocoupling of phenylacetylene at 60 °C for 24 h under air to give 1,4-diphenylbuta-1,3-diyne in 96% yield (eq. 1).



To demonstrate the extent of substrate tolerance in this catalytic system, the reaction of various alkynes was investigated (Scheme 2). The reaction of phenylacetylenes bearing various substituents at the *para*-position gave the corresponding 1,3-diynes in up to 99% yield. The reaction of phenylacetylenes bearing *ortho* and *meta*-substituents also underwent the reaction to give the corresponding products in good to excellent yields. Less reactive aliphatic alkynes were also converted the corresponding 1,3-diynes, although longer reaction time (48 h) was required. Recyclability of the immobilized copper catalyst was investigated. In the oxidative homocoupling of phenylacetylene, the catalyst was recovered by simple filtration and reused eight times without significant loss of catalytic activity. The

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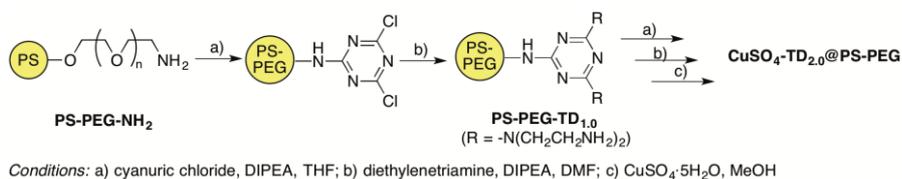
effective copper species still remained in the polymer matrix after 9th cycle, although ICP analysis showed slight leaching of copper for each recycling run.



Scheme 2. Oxidative homocoupling of terminal alkynes

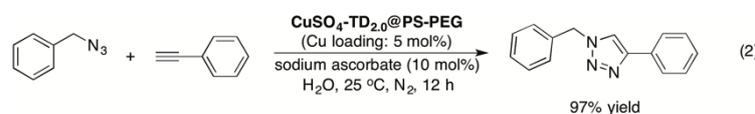
Chapter 2

The author described development of polystyrene-poly(ethylene glycol) resin-supported triazine-based dendrimer-copper catalyst and the application to the Huisgen 1,3-dipolar cycloaddition. The polystyrene-poly(ethylene glycol) (PS-PEG) resin-supported triazine-based dendrimer-copper sulfate ($\text{CuSO}_4\text{-TD}_{2.0}\text{@PS-PEG}$) was prepared according to Scheme 3. The PS-PEG-supported triazine-based dendrimer and the supported copper catalyst were characterized by FT-IR spectroscopies, FE-SEM and ICP-AES.



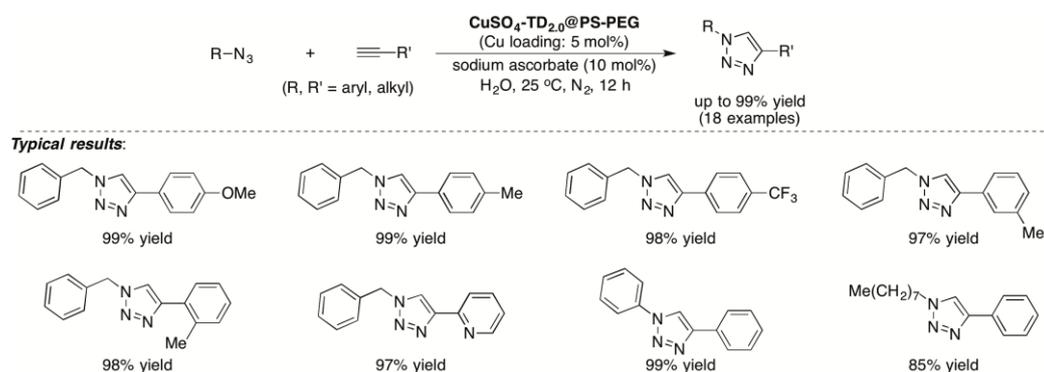
Scheme 3. Preparation of $\text{CuSO}_4\text{-TD}_{2.0}\text{@PS-PEG}$

When $\text{CuSO}_4\text{-TD}_{2.0}\text{@PS-PEG}$ was applied to the Huisgen 1,3-dipolar cycloaddition of phenylacetylene and benzyl azide in water at 25 °C for 12 h, the desired triazole was obtained in 97% yield (eq. 2).



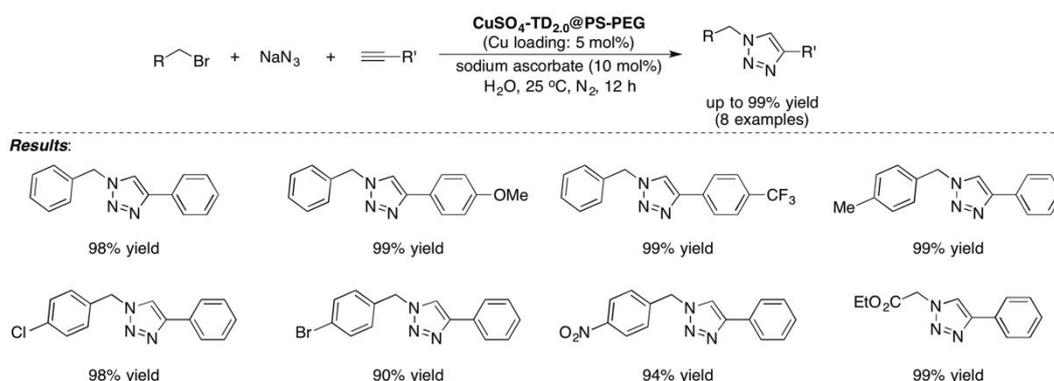
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To demonstrate the substrate tolerance in this catalytic system, the substrate scope was investigated (Scheme 4). Various aromatic and aliphatic alkynes bearing a wide range of electronic properties and functionalities underwent the Huisgen 1,3-dipolar cycloaddition reaction with benzyl azide to give the corresponding 1,4-disubstituted-1,2,3-triazoles in up to 99% yield. Various aromatic, benzylic and aliphatic azides were also applicable, giving the corresponding 1,4-disubstituted-1,2,3-triazoles in 85-99% yield. In the Huisgen 1,3-dipolar cycloaddition reaction of phenylacetylene with ethyl azidoacetate, the catalyst was recovered by simple filtration and reused seven times without significant loss of catalytic activity.



Scheme 4. Huisgen 1,3-dipolar cycloaddition of organic azides with alkynes

$\text{CuSO}_4\text{-TD}_{2.0}\text{@PS-PEG}$ also promoted the three-component reaction of alkynes, alkyl bromides, and sodium azide to afford the corresponding 1,2,3-triazoles in up to 99% yield (Scheme 5).



Scheme 5. Three-component cyclization of alkyl bromides, sodium azide, and alkynes

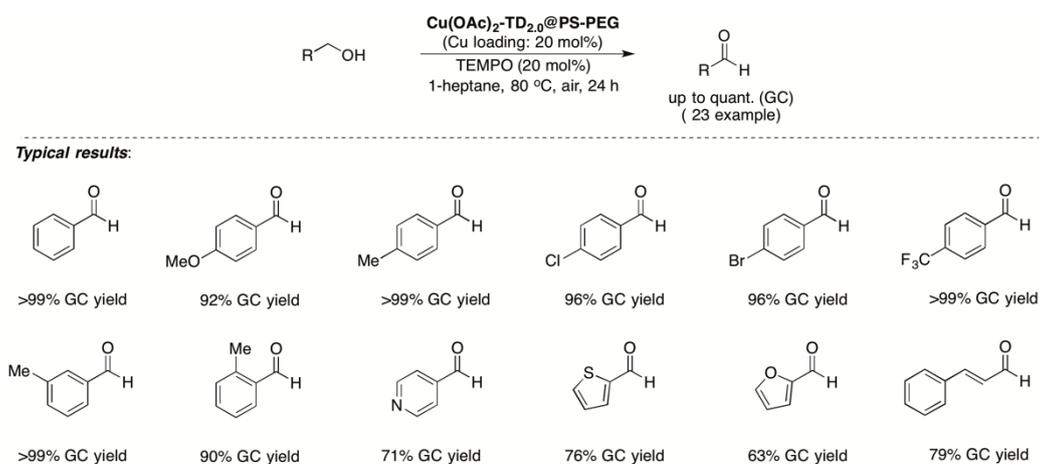
Chapter 3

The author described further application of polystyrene-poly(ethylene glycol) resin-supported triazine-based dendrimer-copper catalyst to the aerobic oxidation of alcohols. The polystyrene-poly(ethylene glycol) (PS-PEG) resin-supported triazine-based dendrimer-copper acetate [$\text{Cu}(\text{OAc})_2\text{-TD}_{2.0}\text{@PS-PEG}$] was prepared with

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$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ following the similar procedure in Scheme 3. The supported copper catalyst was characterized by FE-SEM and ICP-AES.

$\text{Cu}(\text{OAc})_2\text{-TD}_{2.0}\text{@PS-PEG}$ exhibited high catalytic activity for selective aerobic oxidation of alcohols to aldehydes in the presence of a catalytic amount of TEMPO under air atmosphere (Scheme 6). Various benzylic alcohols bearing a wide range of electronic properties and functionalities underwent the aerobic oxidation to give the corresponding aldehydes in up to quantitative GC yield. Cinnamyl alcohol was also applicable for the reaction, giving cinnamyl aldehyde in 79% yield. In the oxidation of benzylic alcohol, the catalyst was recovered and reused four times without significant loss of catalytic activity.



Scheme 6. Aerobic oxidation of alcohols to aldehydes

In conclusion, the author has developed polystyrene-based resin-supported copper catalysts for the aerobic oxidative homocoupling of terminal alkynes, the Huisgen 1,3-dipolar cycloaddition reaction of alkynes with organic azides, and aerobic oxidation of benzylic alcohols. The immobilized copper catalysts could be readily recovered and reused for several times without significant loss of their catalytic activities. These organic reaction systems using the heterogeneous copper catalysts supported polystyrene-based resins achieved not only efficient organic transformations with high recyclability, but also replacement of precious transition-metals with ubiquitous transition-metals. The achievement of this research provides new methodology for the synthesis of various organic compounds with high green-sustainability in academia and industry.

Summary of the results of the doctoral thesis screening

近年、高効率反応を実現するのみならず、高いグリーンサステナビリティを兼ね備えた遷移金属触媒による有機分子変換反応の開発が大きな関心を集めている。これまで開発されている遷移金属触媒反応は、触媒の回収・再利用が困難な均一系触媒である。触媒金属種として地球埋蔵量が少なく、高価なパラジウムやプラチナなどの貴金属を用いていることが多く、グリーンサステナビリティを十分に満たすためには課題が残されている。それらの問題点を解決すべく、出願者は、地球埋蔵量が多く、安価な銅に着目し、簡便な触媒の回収・再利用が可能となる不均一系銅触媒、特に、新規ポリスチレン高分子担持銅触媒の開発を行っている。ポリスチレン担持銅触媒の開発を通じて、高効率グリーンサステナブル有機分子変換反応の実現を目指している。

本論文は、序論、3章から成る本論、結論で構成されている。

序論では、グリーンサステナビリティの観点を踏まえた従来の遷移金属触媒の問題点、一連のポリマー担持不均一系触媒の先例、ポリスチレン担持銅触媒の開発に至る背景、などが簡潔にまとめられている。

第一章では、ポリスチレン担持 N,N,N',N' -テトラエチルジエチレントリアミン銅(II)錯体触媒の開発について述べられている。出願者は、得られたポリスチレン担持銅錯体が、末端アセチレンの酸化ホモカップリング反応を効率的に触媒し、目的生成物である1,3-ジインを最高99%収率で与えることを見出している。また、本錯体触媒が、濾過により回収・再利用でき、フェニルアセチレンのホモカップリング反応に関して、触媒活性が著しく低下することなく、8回の再利用が可能であることを明らかにしている。

第二章では、ポリスチレン-ポリエチレングリコール担持ポリアミントリアジンデンドリマー銅(II)錯体触媒の開発について述べられている。出願者は、得られたポリスチレン-ポリエチレングリコール担持銅錯体が、水中におけるヒュスゲン1,3-双極子環化付加反応を触媒し、目的生成物である1,2,3-トリアゾールを良好な収率で与えることを見出している。また、本錯体触媒が濾過により回収・再利用でき、フェニルアセチレンとエチルアジドアセテートとの反応に関して、触媒活性が著しく低下することなく、7回の再利用が可能であることを明らかにしている。

第三章では、第二章で得たポリスチレン-ポリエチレングリコール担持ポリアミントリアジンデンドリマー銅(II)錯体触媒を用いたベンジルアルコール類の酸素酸化反応について述べられている。出願者は、触媒量のTEMPO存在下、本触媒が一連のベンジルアルコールを酸素酸化し、生成物としてベンズアルデヒドを良好な収率で与えることを明らかにしている。本ベンジルアルコールの酸素酸化反応においても、使用した触媒は濾過により回収可能であり、著しい触媒活性の低下がみられることなく、4回の再利用が可能であることを明らかにしている。

結論では、論文全体を総括している。

(別紙様式 3)

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以上、開発した一連のポリスチレンポリマー担持銅錯体触媒は、高効率で高いグリーンサステナビリティを満たす有機分子変換反応を実現していることから、当該分野の研究の発展に大きく寄与するものと期待される。また、本論文の成果の一部は、既に一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判断される。

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。