アカデミックプログラム［Ｂ講演］ | 10. 有機化学—有機金属化合物：口頭Ｂ講演

2024年3月18日(月) 13:00 ~ 15:40 E1112(11号館 [1階] 1112)

[E1112-1pm] 10. 有機化学—有機金属化合物

座長：伊藤 繁和、山本 武司

日本語

13:00 ~ 13:20

[E1112-1pm-01]

動的らせん高分子骨格を有するキラリティ可変ホスホロアミダイト配位子の開発

○松本 祐輔[1]、藤江 峻也[1]、山本 武司[1]、杉野目 道紀[1] (1. 京都大学)

英語

13:20 ~ 13:40

[E1112-1pm-02]

銅触媒を用いた1-トリフルオロメチルチオアルケンのヒドロホウ素化およびヒドロアリル化

○小島 有貴[1]、平野 康次[1] (1. 阪大院工)

英語

13:40 ~ 14:00

[E1112-1pm-03]

高い酸化力を有する銅光酸化還元触媒によるスチレンの逆マルコフニコフ型水和反応

○奥 直樹[1]、福家 啓仁[2]、山崎 賢[2]、松井 康哲[3]、池田 浩[3]、三浦 智也[2] (1. 京大院工、2. 岡山大院環境生命自然、3. 阪公大院工)

14:00 ~ 14:20

休憩

英語

14:20 ~ 14:40

[E1112-1pm-04]

電子不足CpIr(III)触媒を利用した位置選択的なC-H官能基化の研究

○平田 裕己[1,3]、木邨 俊介[2]、東田 皓介[3]、吉野 達彦[1]、松永 茂樹[3,1] (1. 北大院薬、2. 京大理、3. 京大院理)

英語

14:40 ~ 15:00

[E1112-1pm-05]

Rh/ルイス酸性金属協働触媒による$C(sp^3)$–O 結合の還元的シリル化反応

○関 凜[1]、城戸 春香[1]、黄 嘉名[2]、井元 郁[2]、三浦 大樹[2]、中尾 佳亮[1] (1. 京都大学　、2. 東京都立大学)

英語

15:00 ~ 15:20

[E1112-1pm-06]

Rh触媒を用いた[2+2+2]環化付加反応による含フッ素四置換不斉炭素の構築

○濱田 慎太郎[1]、小宮 由信[1]、鈴木 俊介[1]、野上 純太郎[1]、佐藤 悠[1]、永島 佑貴[1]、田中 健[1] (1. 東工大物質理工)

英語

15:20 ~ 15:40

[E1112-1pm-07]

ロジウム錯体触媒存在下、*N*-メトキシベンズアミドと *in situ* で発生したヨードニウムイリドとの連続反応によるイソクマリンおよびイソキノロン誘導体の化学選択的合成法の開発

○金 東映[1]、三浦 理紗子[1]、木村 祐[1]、近藤 輝幸[1] (1. 京大)

動的らせん高分子骨格を有する キラリティ可変ホスホロアミダイト配位子の開発

（京大院工）○松本 祐輔・藤江 峻也・山本 武司・杉野目 道紀

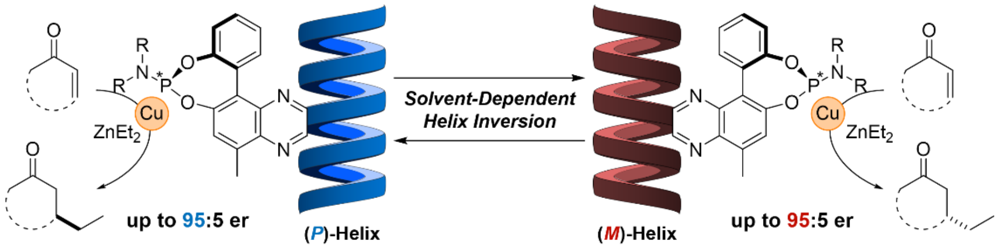
Chirality-Switchable Phosphoramidite Ligands Attached to Helical Poly(quinoxaline-2,3-diyl)s

(*Graduate School of Engineering, Kyoto University*) ○Yusuke Matsumoto, Takaya Fujie, Takeshi Yamamoto, Michinori Suginome

Chiral phosphoramidite is one of the most privileged classes of ligand in asymmetric catalysis.[1] We previously reported chirality-switchable monophosphine and bipyridine ligands attached to dynamic helical poly(quinoxaline-2,3-diyl)s (PQXs), whose helicity can be controlled by solvents.[2] In this work, PQX-based chiral phosphoramidite ligands **PQXpham** were synthesized by post-polymerization functionalization of PQXs bearing diol units. The **PQXpham** served as chirality-switchable ligands in copper-catalyzed asymmetric conjugate addition reaction.

Keywords: Polyquinoxaline; Polymer Ligands; Post-polymerization Functionalization; Copper Catalysis; Asymmetric Conjugate Addition Reaction

キラルなジオールとアミンから合成されるホスホロアミダイトは、不斉遷移金属触媒反応において最も有効なキラル配位子の一つであり、新たな分子設計に基づいた高機能化が期待される[1]。当研究室では、キラル側鎖を有するポリ（キノキサリン-2,3-ジイル）（PQX）の溶媒による主鎖らせん不斉制御を報告しており、PQX に単座ホスフィンやビピリジン部位を導入することで立体選択性をスイッチングできるキラルらせん高分子配位子を開発している[2]。今回我々は、ジオール部位を導入した PQX の重合後修飾を行うことで、様々なアミノ基が置換したホスホロアミダイト部位を有するキラルらせん高分子配位子 (**PQXpham**)を新たに開発した。右巻きの(*P*)-**PQXpham** を配位子として用いて銅触媒による不斉共役付加反応を行ったところ、最高で 99% 収率、95:5 er の立体選択性で生成物が得られた。また、溶媒によるらせん反転によって調製した左巻きの(*M*)-**PQXpham** を用いると立体選択性が逆転し、もう一方の鏡像体が得られた。**PQXpham** の配位部位構造を模した低分子モデル配位子では、リン原子上の不斉中心は立体選択性にほとんど影響を与えなかったことから、高分子主鎖のキラルらせん構造が反応の立体選択性に大きく寄与することが示された。



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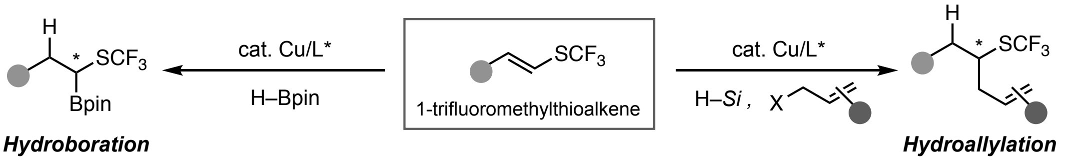
Copper-Catalyzed Hydroboration and Hydroallylation of 1-Trifluoromethylthioalkenes

(*Graduate School of Engineering, Osaka University*) ○Yuki Kojima, Koji Hirano

Keywords: Copper Catalysts; Hydroboration; Hydroallylation; Organofluorine Compounds; Trifluoromethylthio Group

Since their enhanced lipophilicity, metabolic stability, and bioavailability, organofluorine derivatives are an important class of compounds in medicinal chemistry. In particular, trifluoromethylthio (SCF_3) group has received significant attention in the design and synthesis of pharmaceuticals and agrochemicals because of its strong electron-withdrawing nature and high lipophilicity.[1] Although various methods for the synthesis of SCF_3-containing compounds have been reported,[2] it is still difficult to obtain optically active SCF_3 derivatives with high enantiopurity. Therefore, the development of efficient synthetic methods for chiral SCF_3 molecules is highly desired.

Herein, we report a copper-catalyzed regio- and enantioselective hydroboration of 1-trifluoromethylthioalkenes with pinacolborane (H–Bpin). 1-Trifluoromethylthioalkenes can be easily prepared from the corresponding alkenyl halides according to the literature methods.[3] Using the 1-trifluoromethylthioalkene as a starting platform, the in-situ generated copper hydride species undergoes the regio- and enantioselective insertion to form an optically active α-SCF_3 alkylcopper intermediate. Subsequent σ-bond metathesis with H–Bpin provides the boron-substituted SCF_3 compound in an enantioenriched form. Moreover, the copper hydride-based strategy can also be expanded to the three-component coupling reaction of 1-trifluoromethylthioalkenes, hydrosilanes, and allylic electrophiles. Also in this reaction, the judicious choice of chiral ligand induces the high regio- and enantioselectivity. These approaches can provide the chiral SCF_3 compounds, which are difficult to prepare by other means.



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高い酸化力を有する銅光酸化還元触媒によるスチレンの逆マルコフニコフ型水和反応

（京大院工[1]・岡山大院環境生命自然[2]・阪公大院工[3]）○奥 直樹[1]・福家 啓仁[2]・山崎 賢[2]・松井 康哲[3]・池田 浩[3]・三浦 智也[2]

Copper Photoredox Catalyst Exhibiting Strong Oxidizing Ability for *anti*-Markovnikov Hydration of Styrenes

([1]*Graduate School of Engineering, Kyoto University*, [2]*Graduate School of Environmental, Life, Natural Science and Technology, Okayama University*, [3]*Graduate School of Engineering, Osaka Metropolitan University*) ○Naoki Oku,[1] Keito Fuke,[2] Ken Yamazaki,[2] Yasunori Matsui,[3] Hiroshi Ikeda,[3] Tomoya Miura[2]

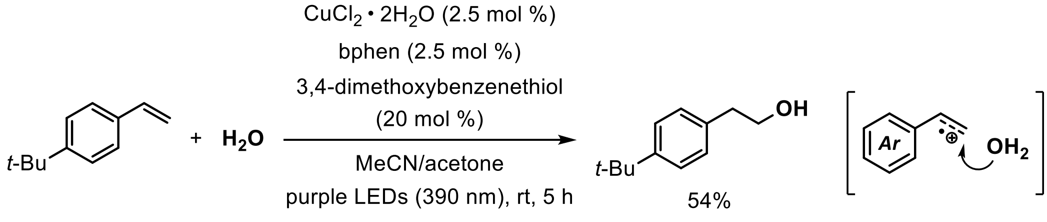
Photoredox catalysts have regained the spotlight in organic synthesis. Photoexcited catalysts act as either single-electron oxidants or reductants, generating radical ions from various organic molecules. In terms of availability and cost, the development of photoredox catalysts using abundant first-row transition metals is highly required. Here, we report a copper photoredox catalyst exhibiting strong oxidizing ability and its application to *anti*-Markovnikov hydration of styrenes.

A mixture of 4-*tert*-butylstyrene, $CuCl_2 \cdot 2H_2O$ (2.5 mol %), bathophenanthroline (bphen; 2.5 mol %), and 3,4-dimethoxybenzenethiol (20 mol %) in MeCN/acetone/H_2O (5:5:1, 4.5 mL) was irradiated with purple LEDs (390 nm) at ambient temperature. After 5 hours, the primary alcohol was formed in 60% NMR yield. Purification by preparative thin-layer chromatography gave the product in 54% isolated yield. Single-electron oxidation of styrenes proceeds by the photoexcited copper catalyst. The generated radical cations undergo a direct addition of H_2O in an *anti*-Markovnikov manner to furnish the desired alcohols.

Keywords : Copper; Photoredox Catalysis; Radicals; Hydration; anti-Markovnikov Addition

可視光酸化還元触媒は、その光励起状態が一電子酸化剤あるいは還元剤として働くことで、簡便にさまざまなラジカルイオンを発生できることが知られている。そのため入手コストの観点から、安価で入手容易な第一遷移金属を用いた光酸化還元触媒の開発は重要な研究課題である。我々は新たに開発した銅可視光酸化還元触媒を用いるスチレン類の逆マルコフニコフ型水和反応を見出したので報告する。

銅触媒およびチオール触媒の存在下、4-*tert*-ブチルスチレンをアセトニトリル/アセトン/水溶媒中、室温で可視光（390 nm）を照射しながら撹拌すると、目的の 1 級アルコールが収率 54%で得られた。本反応は光励起された銅触媒によるスチレンの一電子酸化で生じたラジカルカチオン種に対し、水が逆マルコフニコフ選択的に付加することで進行すると考えている。

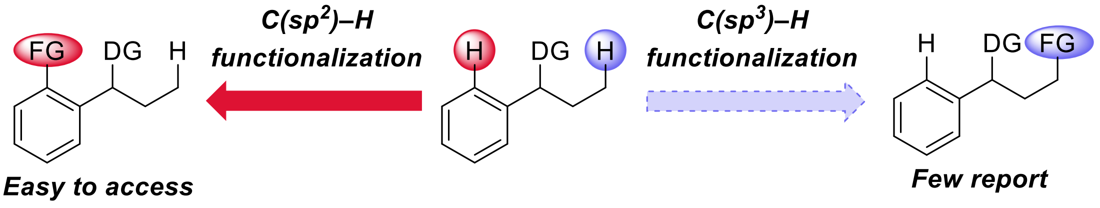


Site-selective C–H functionalization catalyzed by electron-deficient CpIr(III) catalyst

([1]*Grad. Sch. Pharm. Sci. Hokkaido Univ.*, [2]*Fac. Sci., Kyoto Univ.*, [3]*Grad. Sch. Sci. Kyoto Univ.*)
○ Yuki Hirata[1,3], Shunsuke Kimura[2], Kosuke Higashida[3], Tatsuhiko Yoshino[1], Shigeki Matsunaga[1,3]

Keywords: C–H activation, iridium catalyst

Direct C–H functionalization of inert C–H bond is known as a convenient tool that enable step- and atom-economical synthesis of various organic molecules. Group 9 transition metals (Co, Rh, Ir) bearing cyclopentadienyl ligands (Cp) show high reactivity to C–H functionalization. The mechanism of CpM(III) catalyzed C–H activation is generally proposed to proceed via concerted-metallation deprotonation (CMD), which is a concerted mechanism for hydrogen to be abstracted as a proton by a weak base such as a carboxylate. Generally, C(sp^2)–H bond cleavage step is supposed to proceed more easily than C(sp^3)–H bond due to various factor, mainly difference of Bond Dissociation Energy (BDE) and acidity of C–H bond. Therefore, C(sp^3)-H functionalization is fewer than C(sp^2)-H functionalization. In addition, when a substrate that has both C(sp^2) and C(sp^3)–H bond on accessible sites for C–H activation is used, the product from C(sp^2)–H activation or the mixture of C(sp^2) and C(sp^3)–H functionalized product or both was obtained due to C(sp^2)–H functionalization prior to C(sp^3)–H. Thus, site-selective C(sp^3)–H functionalization has been challenging, and the achievement of selective C(sp^3)–H functionalization is highly demanded towards flexible modification of molecules. Recently, several site-selective C(sp^3)–H functionalization was reported. Yu's group achieved selective C(sp^3)–H iodination by chelation-control in 2017.1) In 2018, Xu's group enabled to control its selectivity by the number of atoms in metallacycle.2) However, these reports depended on the structure of a substrate, and flexible and switchable C(sp^3)–H functionalization of compounds that have both C(sp^2) and C(sp^3)–H bond, has not been achieved by high-valent metal catalysis. Here in, we demonstrate flexible and switchable C(sp^3)–H functionalization catalyzed by electron-deficient CpIr(III) catalyst. Substrate scope as well as synthetic application will be explained in this presentation.



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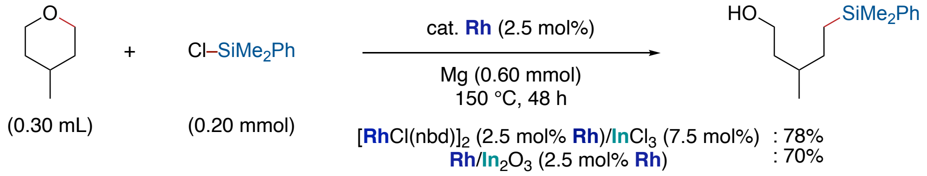
Reductive $C(sp^3)$–O Silylation by Cooperative Rhodium/Lewis Acidic Metal Catalysis

(*[1]Department of Material Chemistry, Graduate School of Engineering, Kyoto University, [2]Department of Applied Chemistry for Environment, Graduate School of Urban Environmental Science, Tokyo Metropolitan University)* ○Rin Seki,[1] Haruka Kido,[1] Kana Ko,[2] Kaoru Imoto,[2] Hiroki Miura,[2] Yoshiaki Nakao[1]

Keywords: $C(sp^3)$–O bond, silylation, rhodium, Lewis acids, Cooperative catalysis

Alcohol and ethers represent ubiquitous structural motifs in both feedstock and fine chemicals. Abundant biopolymers such as cellulose and lignin, characterized by their primary skeletons composed of multiple C–O bonds, are anticipated as sources for organic compounds. Furthermore, the industrial synthetic process for alcohols and ethers has been established. C–O bond transformations directly edit the main skeleton of these molecules and allow access to a wide range of molecules from simple feedstock. However, the formidable chemical stability of alcohols and ethers, arising from the diminished leaving group ability of alkoxides and hydroxides, makes this difficult. Conventional transformations of alcohols and ethers have heavily relied on conversion to more facile leaving groups, such as sulfonates and phosphates, and the direct conversion of C–OR (R = alkyl, H) bonds has proven to be intricate. Recently, the Dong group[1] and the Miura and Shishido group[2,3] have reported the $C(sp^3)$–O bond functionalization of alkyl ethers. As elucidated above, this type of transformation has garnered substantial attention recently.

We have found that reductive $C(sp^3)$–O silylation catalyzed cooperatively by rhodium and Lewis acidic metals in the presence of magnesium powder. For instance, the reaction of 4-methyltetrahydropyrane (0.30 mL) with chlorodimethylphenylsilane (0.20 mmol) in the presence of $[RhCl(nbd)]_2$ (2.5 mol%), $InCl_3$ (7.5 mol%), and magnesium powder (0.60 mmol) afforded the ring-opened and $C(sp^3)$–O silylated product in 78% yield. We also found that rhodium nanoparticles supported on indium oxide catalyzed the same type of transformation. Experiments have suggested that the reaction is catalyzed by nanoparticles containing multi-metallic species in both conditions. We will present the results focusing on chemo-selectivity and the reaction mechanism.



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Enantioselective construction of tetrasubstituted fluorine stereocenters by Rh-catalyzed [2+2+2] cycloaddition reaction

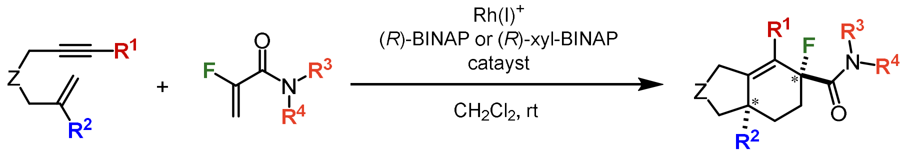
([1]*Department of Chemical Science and Engineering, Tokyo Institute of Technology*)
○Shintaro Hamada,[1] Yoshinobu Komiya,[1] Shunsuke Suzuki,[1] Juntaro Nogami,[1] Yu Sato,[1] Yuki Nagashima,[1] Ken Tanaka[1]

Keywords: *cycloaddition, C-H activation, Rhodium, fluorine*

The asymmetric construction of tetrasubstituted fluorine stereocenter is one of the most synthetically challenging areas. Although asymmetric C–F bond formation using fluorination reagents and asymmetric C–C bond formation of fluorinated compounds by nucleophilic or coupling reactions have been developed, asymmetric cycloaddition reactions of fluoroalkenes have been limited in only three reports [1].

On the other hand, our group has reported that acrylamide derivatives, which have higher coordination ability than enones and acrylates, are excellent substrates for addition reactions catalyzed by cationic Rh(I) complexes. We have established the enantioselective [2+2+2] cycloaddition reaction with acrylamides and 1,6-enynes proceeded smoothly to give chiral cyclohexene derivatives in high yields and high ee's [2].

In this presentation, we report an efficient method for constructing chiral fluorinated cyclohexene derivatives by the Rh(I)-catalyzed [2+2+2] cycloaddition reaction with fluoroacrylamides and 1,6-enynes. Detailed investigations revealed that C–H activation of acrylamides proceeds as a side reaction, and substituents and ligands control these cycloaddition and C–H activation reactions.



1

2
(1.2 equiv)

3
up to 84% yield, >99% ee

✓Enantioselective construction of tetrasubstituted fluorine stereocenter
✓High yields and high ee's
✓Substituents and Ligand controlled reaction mechanism

References:

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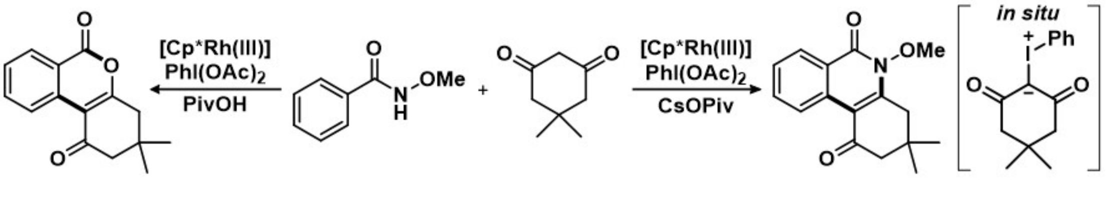
Chemodivergent Synthesis of Isocoumarins and Isoquinolones by Rhodium-catalyzed Consecutive Reaction of *N*-Methoxybenzamide with *in situ* Generated Iodonium Ylides

(*Graduate School of Engineering, Kyoto University*) ○Dongyoung Kim, Risako Miura, Yu Kimura, Teruyuki Kondo

Keywords: Rhodium; C-H activation; Heterocyclization; Isocoumarin; Isoquinolone

Over the past decade, transition metal-catalyzed direct C-H bond activation, insertion, and annulation reactions using diverse carbene precursors such as diazo compounds, sulfoxonium ylides, iodonium ylides, and others have been developed for the synthesis of various heterocyclic compounds.[1] However, almost all reactions required the preparation of carbene precursors from 1,3-dicarbonyl compounds in advance. In addition, attempts to use only 1,3-dicarbonyl compounds for catalytic construction of diverse heterocyclic scaffolds have been failed. In 2020, Li and co-workers first reported that Rh-catalyzed coupling reaction of benzoic acids with 1,3-dicarbonyl compounds gave isocoumarins, selectively, in which the generated iodonium ylides would give a carbene species.[2] Thus, the development of environmentally benign and atom-efficient catalytic synthesis of heterocyclic compounds using *in situ* generated carbene species from simple 1,3-dicarbonyl compounds is highly demanded.[3]

In a continuation of our study on catalytic synthesis of several *N*-heterocyclic compounds via C(sp^2)-H bond activation, we succeeded in developing novel Rh-catalyzed consecutive reaction, which consists of catalytic cleavage of C(sp^2)-H bond of *N*-methoxybenzamide to give a five-membered rhodacyclic intermediate, and insertion of *in situ* generated carbene species by only mixing 1,3-diketones with (diacetoxyiodo)benzene, followed by two-kinds of distinct intramolecular cyclization, enabled chemodivergent synthesis of isocoumarins and isoquinolones in one-pot. The two-kinds of distinct intramolecular cyclization pathways could be controlled, completely, by appropriate use of either Lewis acids (for isoquinolones) or carboxylic acids (for isocoumarins) in the presence of the same [Cp*RhCl$_2$]$_2$ catalyst.



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