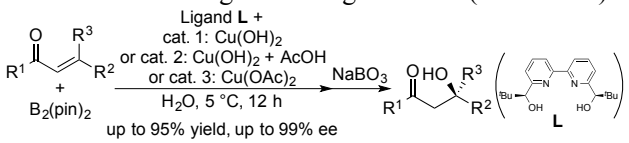
SYNTHETIC ORGANIC CHEMISTRY

Annual Research Highlights

(1) Heterogeneous versus Homogeneous Copper(II) Catalysis in Enantioselective Conjugate-Addition Reactions of Boron in Water

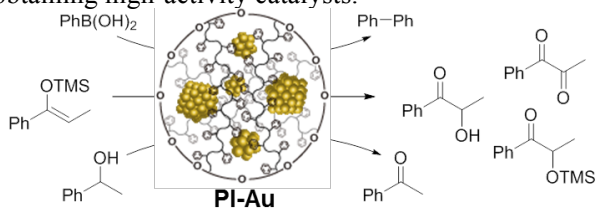
We have developed Cu^{II}-catalyzed enantioselective conjugate-addition reactions of boron to α,β-unsaturated carbonyl compounds and α,β,γ,δ-unsaturated carbonyl compounds in water. In contrast to our previously reported Cu^{I} catalysis that required organic solvents, chiral Cu^{II} catalysis was found to proceed efficiently in only water. The catalyst gave high yields and enantioselectivities with some substrates and also gave the highest TOF (43200 h^{-1}).



Scheme 1 Copper(II)-catalyzed Enantioselective Conjugate-Addition Reactions of Boron in Water
1.(1)-1) *Chem. Asian J.* **9**, 179 (2014)

(2) Preparation of polymer incarcerated gold nanocluster catalysts (PI-Au) and their application to aerobic oxidation reactions

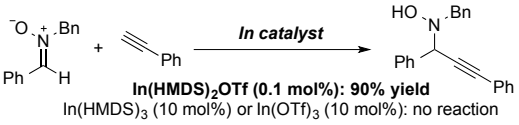
Heterogeneous gold nanocluster catalysts immobilized by the method known as polymer incarceration were prepared. The catalysts prepared could be applied to the aerobic oxidation of phenyl boronic acids, alcohols, and silyl enol ethers. We found that the choice of polymers, good and poor solvents for the polymers, metal loadings, heating conditions for cross-linking, and final activation were all crucial for obtaining high-activity catalysts.



Scheme 2 PI-Au catalyzed aerobic oxidation reactions
1.(1)-8) *Tetrahedron.* **70**, 6039 (2014)

(3) A Lewis acid/metal amide hybrid as an efficient catalyst for carbon–carbon bond formation

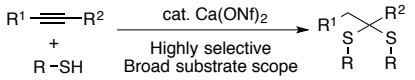
While Lewis acids and metal amides are among the most frequently used metal species, they are believed to be incompatible when combined. Here we describe a Lewis acid/metal amide hybrid, which contains electron-withdrawing groups and basic and bulky nitrogen functional groups in the same metal complex, as a novel catalyst. We have synthesized $In(N(SiMe_3)_2)_2Cl$ ($In(HMDS)_2Cl$) and $In(HMDS)_2OTf$ which showed excellent catalytic activity for the reaction of nitrones with terminal alkynes.



Scheme 3 $In(HMDS)_2OTf$-catalyzed addition of terminal alkyne to nitrone
1.(1)-10) *Chem. Sci.* **5**, 3958 (2014)

(4) Calcium-Catalyzed Bis-hydrothiolation of Unactivated Alkynes Providing Dithioacetals

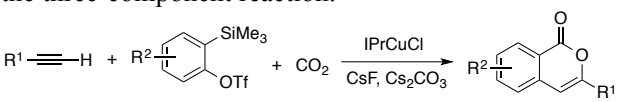
Bis-hydrothiolation of alkynes providing *anti*-Markovnikov dithioacetals is reported. Lewis-acidic $Ca(OSO_2C_4F_9)$ ($Ca(ONf)_2$) was synthesized for the first time and was shown to be an excellent catalyst for the transformation. The reaction is highly selective and has a wide substrate scope.



Scheme 4 Ca-catalyzed Bis-hydrothiolation of Unactivated Alkynes
1.(1)-12) *Organometallics.* **33**, 5626 (2014)

(5) Three-Component Couplings of Arynes, Terminal Alkynes, and CO_2 Catalyzed by an NHC–Copper Complex

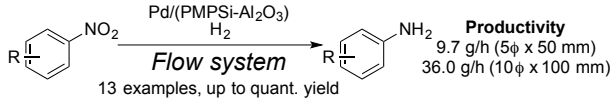
A copper-catalyzed multicomponent coupling reaction between in situ generated *ortho*-arynes, terminal alkynes, and CO_2 was developed to access isocoumarins in moderate to good yields. The key to this CO_2-incorporating reaction was the use of a versatile N-heterocyclic carbene/copper complex that was able to catalyze multiple transformations within the three-component reaction.



Scheme 5 NHC–Copper Complex catalyzed Three-Component Couplings of Arynes, Terminal Alkynes, and Carbon Dioxide
1.(1)-11) *Angew. Chem. Int. Ed.* **53**, 10213 (2014)

(6) Catalytic Flow Hydrogenation of Aromatic Nitro Compounds

Continuous-flow hydrogenation of aromatic nitro compounds was successfully performed by using polysilane-supported palladium catalysts to afford the corresponding amino compounds in high yields. Productivity was high, and a wide variety of nitro compounds were applicable under the continuous-flow conditions.



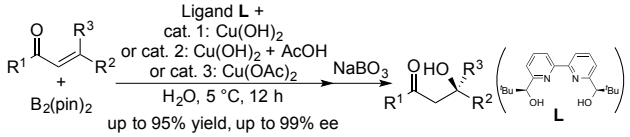
Scheme 6 Catalytic Flow Hydrogenation of Aromatic Nitro Compounds Using Polysilane-Supported Palladium
1.(1)-14) *J. Flow Chem.* **4**, 160 (2014)

有機合成化学研究室

研究ハイライト

(1) 水中不斉ホウ素共役付加反応における均一系及び不均一系銅(II)触媒の比較

今回筆者らは、銅(II)触媒による α, β-不飽和カルボニル化合物類及び α, β, γ, δ-不飽和カルボニル化合物類への水中不斉ホウ素共役付加反応を開発した。以前我々が報告した有機溶媒を必要とした銅(I)触媒系と異なり、不斉銅(II)触媒系は水中でのみ効果的に機能する事を見出した。本触媒系は様々な基質に対し高収率・高エナンチオ選択性を示し、TOF 最高で 43200 h^{-1} であった。



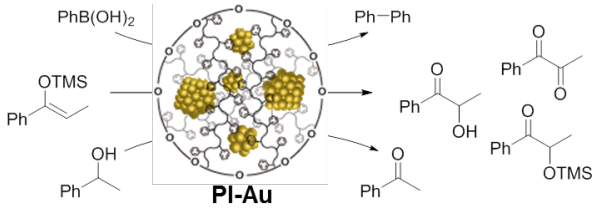
Copper(II)-catalyzed Enantioselective Conjugate-Addition Reactions of Boron in Water

式１　銅(II)触媒による水中不斉ホウ素共役付加反応

1.(1)-1) *Chem. Asian J.* **9**, 179 (2014)

(2) 高分子カルセランド型金ナノクラスター触媒の酸素酸化反応への応用

不均一系金ナノクラスター触媒を、高分子カルセランド法により調製し、アリールボロン酸類、アルコール類、シリルエノールエーテル類の酸素酸化反応に応用した。今回我々は、高分子の種類、高分子に対する良溶媒・貧溶媒、金属担持量、架橋反応における加熱条件、最終的な活性化法の選択全てが触媒の高活性を維持するのに重要であることを見出した。

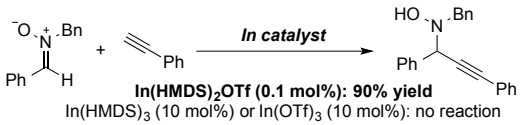


式２　PI-Au 触媒による酸素酸化反応

1.(1)-8) *Tetrahedron.* **70**, 6039 (2014)

(3) ルイス酸/金属アミドハイブリッド型触媒による炭素－炭素結合生成反応の開発

ルイス酸類及び金属アミド類は最も頻繁に使用される金属種であるが、両方を混合すると互いに共存出来ないと考えられてきた。今回我々は電子求引基と塩基性かつ嵩高い窒素官能基を同一錯体中に含む、ルイス酸/金属アミドハイブリッド型触媒を開発した。我々は $In(N(SiMe_3)_2)_2Cl$、$(In(HMDS)_2Cl)$及び $In(HMDS)_2OTf$ を合成し、これらが末端アルキン類のニトロン類に対する付加反応に対し非常に高活性な触媒である事を示した。

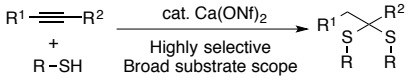


式３　ハイブリッド型インジウム触媒による末端アルキン類のニトロン類に対する付加反応

1.(1)-10) *Chem. Sci.* **5**, 3958 (2014)

(4) ジチオアセタール類を与えるカルシウム触媒による不活性アルキン類に対するビスヒドロチオール化

アンチマルコフニコフ型ジチオアセタール類を与えるアルキン類のビスヒドロチオール化を報告する。ルイス酸性である $Ca(OSO_2C_4F_9)$ $(Ca(ONf)_2)$を初めて合成し、本反応に有効に機能する触媒である事を示した。本反応は高い選択性と広い基質一般性を示した。

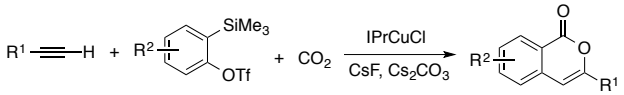


式４　カルシウム触媒による不活性アルキン類に対するビスヒドロチオール化

1.(1)-12) *Organometallics.* **33**, 5626 (2014)

(5) NHC-銅錯体によるアライン類、末端アルキン類、二酸化炭素の三成分カップリング反応

銅触媒による系中発生させたオルト-アライン類、末端アルキン類、二酸化炭素の多成分カップリング反応を開発し、イソクマリン類を中程度から良好な収率で得た。三成分連結反応における多数の変換を触媒可能な *N*-ヘテロ環状カルベン-銅錯体を用いる事が本二酸化炭素固定化反応の鍵である。

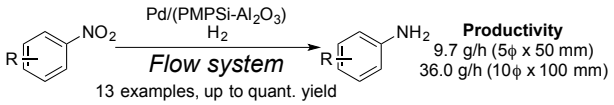


式５　NHC-銅錯体によるアライン類、末端アルキン類、二酸化炭素の三成分カップリング反応

1.(1)-11) *Angew. Chem. Int. Ed.* **53**, 10213 (2014)

(6) 芳香族ニトロ化合物の触媒的水素化フロー反応

ポリシラン固定化パラジウム触媒を用いた芳香族ニトロ化合物の連続的水素化フロー反応の開発に成功し、対応するアミン類を高収率で得た。本連続的フロー条件は、高い生産性を示し、広い範囲のニトロ化合物類に適用可能であった。



Scheme 6 Catalytic Flow Hydrogenation of Aromatic Nitro Compounds Using Polysilane-Supported Palladium

式６　ポリシラン固定化パラジウム触媒を用いた芳香族ニトロ化合物の触媒的水素化フロー反応

1.(1)-14) *J. Flow Chem.* **4**, 160 (2014)

1. 原著論文

(1) Refereed Journals

1) Heterogeneous versus Homogeneous Copper(II) Catalysis in Enantioselective Conjugate-Addition Reactions of Boron in Water, T. Kitanosono, P. Xu, S. Kobayashi, *Chem. Asian J.*, **9**, 179-188 (2014).
2) Calcium Chloride ($CaCl_2$) as Catalyst for Asymmetric Organic Reactions, T. Tsubogo, Y. Yamashita, S. Kobayashi, *Topics in Catalysis*, **57**, 935-939 (2014).
3) A Cooperative Water Effect in Proazaphosphatrane-Catalysed Heterocycle Synthesis, M. A. Honey, Y. Yamashita, S. Kobayashi, *Chem. Commun.,* **50***,* 3288-3291 (2014).
4) Tandem Oxidative Processes Catalyzed by Polymer-Incarcerated Multimetallic Nanoclusters with Molecular Oxygen, H. Miyamura, S. Kobayashi, *Acc. Chem. Res.*, **47**, 1054-1066 (2014).
5) Development of Chiral Catalysts for Mukaiyama Aldol Reactions in Aqueous Media, T. Kitanosono, S. Kobayashi, *Chem. Rec.*, **14**, 130-143 (2014).
6) Efficient Visible Light-Mediated Cross-Dehydrogenative Coupling Reactions of Tertiary Amines Catalyzed by a Polymer-Immobilized Iridium-Based Photocatalyst, W.-J. Yoo, S. Kobayashi, *Green Chem.*, **16**, 2438-2442 (2014).
7) Sulfuryl Chloride as an Efficient Initiator for the Metal-Free Aerobic Cross-Dehydrogenative Coupling Reaction of Tertiary Amines, A. Tanoue, W.-J. Yoo, S. Kobayashi, *Org. Lett.*, **16**, 2346-2349 (2014).
8) Preparation of Polymer Incarcerated Gold Nanocluster Catalysts (PI-Au) and their Application to Aerobic Oxidation Reactions of Boronic Acids, Alcohols, and Silyl Enol Ethers, H. Miyamura, T. Yasukawa, S. Kobayashi, *Tetrahedron*, **70**, 6039-6049 (2014).
9) Cu(II)-Catalyzed Asymmetric Boron Conjugate Addition to α,β-Unsaturated Imines in Water, T. Kitanosono, P. Xu, S. Isshiki, L. Zhu, S. Kobayashi, *Chem Comm*., **50**, 9336-9339 (2014).
10) A Lewis Acid/Metal Amide Hybrid as an Efficient Catalyst for Carbon–Carbon Bond Formation, Y. Yamashita, Y. Saito, T. Imaizumi, S. Kobayashi, *Chem. Sci.*, **5**, 3958-3962 (2014).
11) An Efficient Synthesis of Isocoumarins via *N*-Heterocyclic Carbene-Copper Complex Catalyzed Three-Component Coupling Reactions of Arynes, Terminal Alkynes, and Carbon Dioxide, W.-J. Yoo, T. V. Q. Nguyen, S. Kobayashi, *Angew. Chem. Int. Ed.*, **53**, 10213-10217 (2014).
12) Calcium-Catalyzed Bis-Hydrothiolation of Unactivated Alkynes Providing Dithioacetals, M. Huťka, T. Tsubogo, S. Kobayashi, *Organometallics*, **33**, 5626-5629 (2014).
13) Zinc(II) Hexachloroantimonate-Catalyzed Oxidative Allylation of Glycine Derivatives, W.-J. Yoo, A. Tanoue, S. Kobayashi, *Asian J. Org. Chem.*, **3**, 1066-1069 (2014).
14) Catalytic Flow Hydrogenation of Aromatic Nitro Compounds Using Polysilane-supported Palladium, M. Ueno, Y. Morii, K. Uramoto, H. Oyamada, Y. Mori, and S. Kobayashi, *J. Flow Chem*., **4**, 160-163 (2014).

15) Catalytic Imine–Imine Cross-Coupling Reaction, M. Matsumoto, M. Harada, Y. Yamashita, S. Kobayashi, *Chem. Comm*., **50**, 13041-13044 (2014).

16) Catalytic Organic Reactions on the Surface of Silver(I) Oxide in Water, M. Ueno, A. Tanoue, S. Kobayashi, *Chem. Lett.*, **43**, 1867-1869 (2014).

2. 総説・解説

1) Chiral Metal Nanoparticle-Catalyzed Asymmetric C–C Bond Formation Reactions, T. Yasukawa, H. Miyamura, S. Kobayashi, *Chem. Soc. Rev.*, **43**, 1450-1461 (2014).

4. その他

1) 日本経済新聞　2014年5月13日「薬・樹脂の原料　水中で合成　東大・東工大　有害な溶媒使わず」

2) 毎日新聞　2014年12月4日「有機合成「もっと自在に」」