International Research Center for Elements Science – Synthetic Organotransformation –

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Prof
NAKAMURA, Masaharu
(D Sc)

Assoc Prof
TAKAYA, Hikaru
(D Eng)

Assist Prof
ISOZAKI, Katsuhiro
(D Eng)

Assist Prof
IWAMOTO, Takahiro
(D Eng)

PD
PINCELLA, Francesca
(Ph D)

PD
GELDSETZER, Jan
(Ph D)

Researcher (pt)

MATSUDA, Hiroshi

Students

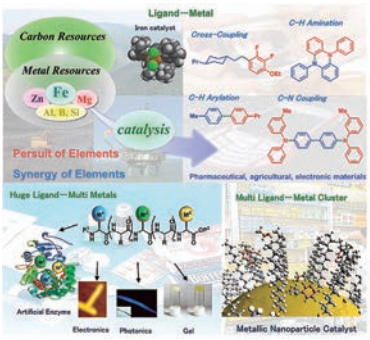
AOKI, Yuma (D3)
AGATA, Ryosuke (D3)
OKUZONO, Chiemi (M2)
UENO, Ryo (M2)
HOSOKAWA, Atsushi (M1)
SHANOH, Takafumi (M1)
LU, Siming (RS)
NOMURA, Satsuki (RS)
IWAKAMI, Mako (UG)
TOYODA, Takahiro (UG)

Guest Res Assoc

BYRNE, Sthephan Ireland Trinity College, Ireland, 30 June–23 August

Scope of Research

Our research activity focuses on the development of new molecular transformations, which can contribute to better or ideal synthesis of functional molecules as well as to exploitation of new chemical (metal and carbon) resources. The present research subjects are (1) metal-catalyzed carbon–carbon and carbon–heteroatom bond forming reactions by using universal metals such as iron (2) development of smart materials based on synergistic effect of various metals on artificial peptides (3) development of smart metallic nanoparticle catalysts based on supramolecular approaches (4) understanding of reaction mechanism of these catalytic reactions with the help of quantum chemical methods and synchrotron X-ray absorption spectroscopy.



KEYWORDS

Selective Organic Reaction
Iron Catalyst
Metalated Peptide Catalyst
Metallic Nanoparticle Catalyst
Solution-Phase XAS Analysis

Selected Publications

Sharma, A. K.; Sameera, W. M. C.; Adak, L.; Jin, M.; Okuzono, C.; Iwamoto, T.; Nakamura, M.; Morokuma, K., DFT and AFIR Study on the Mechanism and the Origin of Enantioselectivity in Iron-Catalyzed Cross-Coupling Reactions, *J. Am. Chem. Soc.*, **139,** 16117-16125 (2017).

Iwamoto, T.; Nishikori, T.; Nakagawa, N.; Takaya, H.; Nakamura, M., Iron-Catalyzed anti-Selective Carbosilylation of Internal Alkynes, *Angew. Chem. Int. Ed.*, **56,** 13298-13301 (2017).

Adak, L.; Kawamura, S.; Toma, G.; Takenaka, T.; Isozaki, K.; Takaya, H.; Orita, A.; Li, H. C.; Shing, T. K. M.; Nakamura, M., Synthesis of Aryl *C*-Glycosides via Iron-Catalyzed Cross Coupling of Halosugars: Stereoselective Anomeric Arylation of Glycosyl Radicals, *J. Am. Chem. Soc.*, **139,** 10693-10701 (2017).

Nakajima, S.; Takaya, H.; Nakamura, M., Iron-catalyzed Methylation of Arylboron Compounds with Iodomethane, *Chem. Lett.*, **46,** 711-714 (2017).

Takaya, H.; Yokoi, T.; Yoshida, R.; Isozaki, K.; Kawakami, T.; Takenaka, T.; Nakamura, M., Synthesis and Structural Analysis of Ruthenium-Bound Norvaline Peptides, *Chem. Lett.*, **46,** 665-668 (2017).

Iron-Catalyzed Cross-Coupling Reactions

Transition-metal-catalyzed carbon–carbon and carbon–heteroatom bond forming reactions are powerful tools for the synthesis of functional molecules. Our group focuses on use of iron as a catalyst, and so far developed a variety of iron-catalyzed cross-coupling reactions, some of which can't be achieved by conventional transition-metal catalysts such as palladium. As a representative example, we developed the first example of iron-catalyzed enantioselective cross-coupling reaction, which enable facile acsess to optically active α-aryl esters from racemic α-chloroesters and aryl Grignard reagents. However, the reaction mechanism and the origin of enantioselectivity remained unclear. Here we performed DFT and AFIR calculations to reveal that the reaction proceeds via a novel $Fe^{I–II–III}$ mechanism, where iron (I) species **A** homolytically cleaves the C–Cl bond of α-chloropropionate substrates and the resulting alkyl radical recombines to the iron center of organoiron (II) intermediates **C** to generate organoiron (III) intermediates **D** (Figure 1). Finally, the iron (III) intermediate undergoes reductive elimination in a stereoselective manner to furnish optically active α-arylpropionates as the corresponding coupling product.

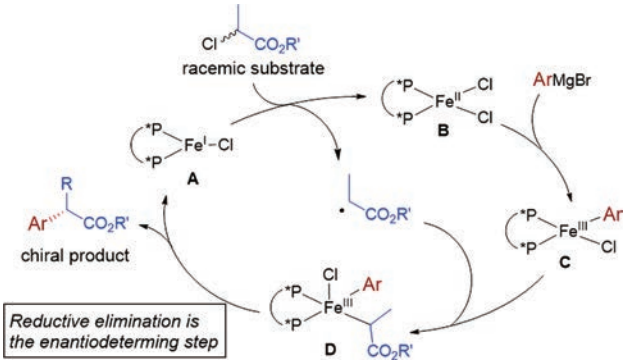


Figure 1. Mechanism of iron-catalyzed enantioselective coupling reaction.

Moreover, we developed diastereoselective iron-catalyzed cross-coupling reaction of various glycosyl halides with aryl metal reagents for the efficient synthesis of aryl *C*-glycosides, which are of significant pharmaceutical interest due to their biological activities and resistance toward metabolic degradation (Figure 2).

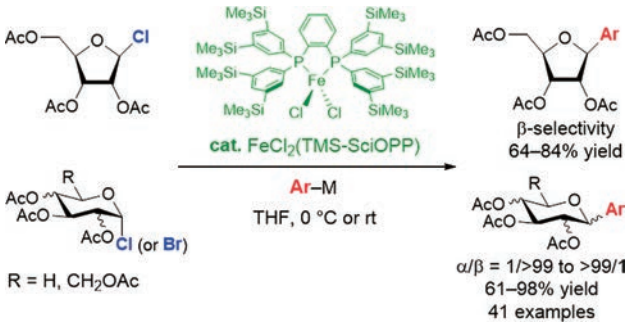


Figure 2. Synthesis of Aryl *C*-Glycosides via Iron-Catalyzed Cross-Coupling of Halosugars.

Novel Transition-Metal Catalyst Bound with Functional Amino Acid or Peptide

This project focuses on development of smart materials based on synergistic effect of various metals on artificial peptides. Based on this concept, we have developed novel ruthenium complex bound with norvaline, which catalyze efficient and selective oxidation of several methoxy-benzene analogues to quinones. Now we are trying further modification of the catalysts toward investigation of future chemical resources.

Supramolecular Approach for Creating Enhanced Catalysis of Metallic Nanoparticles

This project focuses on the development of highly active and selective metallic nanoparticle and cluster catalysts. To achieve this purpose, four key methodologies have been developed: 1) creation of reaction field with advanced self-assembly, 2) design of selective molecular transformation with multi-points intermolecular interaction, 3) size selective synthesis of metallic nanoparticles and clusters, and 4) utilization of plasmonic resonance with light.