

# International Research Center for Elements Science - Organic Main Group Chemistry -

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## Visitors

Prof KÜNDIG, E Peter	University of Genova, Switzerland, 29 May 2008
Prof KOTORA, Martin	Charles University, Czech Republic, 14 July–14 October 2008
Dr YAMADA, Yoichi M. A.	RIKEN, Japan, 6 November 2008
Prof SUZUKI, Akira	Hokkaido University, Japan, 21 November 2008
Prof YAMANAKA, Masahiro	Rikkyo University, Japan, 21 November 2008
Prof MOROKUMA, Keiji	Fukui Memorial Research Institute, Kyoto University, Japan, 9 December 2008

## Scope of Research

Our research activity is focused on the development of molecular transformation reactions, which can provide new ways to exploit chemical resources, such as haloalkanes, alkenes, alcohol etc. The present research subjects are (1) 3d-transition metal catalyzed controlled Carbon–Carbon bond forming reactions which exploit universal metals such as iron, magnesium and aluminum (2) development of smart materials based on synergistic effect of various metals on peptide (3) understanding and design of synergistic effects of multi-element center interactions for the catalysis with the help of quantum chemical methods and spectroscopy.

## Research Activities (Year 2008)

### Publications

Fujimoto T, Endo K, Tsuji H, Nakamura M, Nakamura E: Construction of Chiral Quaternary Carbon Center by Indium-Catalyzed Asymmetric  $\alpha$ -Alkenylation of  $\beta$ -Ketoesters, *J. Am. Chem. Soc.*, **130**, 4492-4496 (2008).

Hatakeyama T, Nakamura M, Nakamura E: Diastereoselective Addition of Zincated Hydrazones to Alkenylboronates and Stereospecific Trapping of Boron/Zinc Bimetallic Intermediates by Carbon Electrophiles *J. Am. Chem. Soc.*, **130**, 15688-15701 (2008).

Hatakeyama T, Yoshimoto Y, Toma G, Nakamura M: Iron-Catalyzed Enyne Cross-Coupling Reaction, *Org. Lett.*, **10**, 5341-5344 (2008).

Hatakeyama T, Kondo Y, Fujiwara Y, Takaya H, Ito S, Nakamura E, Nakamura M: Iron-Catalysed Fluoroaromatic Coupling Reactions under Catalytic Modulation with 1, 2-Bis(diphenylphosphino)benzene, *Chem. Commun.* in press.

### Presentations

Controlling the Iron Catalysis in Cross-Coupling and Some Related Reactions, Nakamura M, The 9th Youngnam-Kinki Joint Symposium on Organometallic Chemistry, Katsura, Kyoto, 24 January 2008.

Controlling Iron-Catalysis in Selective Carbon-Carbon Bond Formations, Nakamura M, The 3rd International

## Enyne Cross-Coupling

Transition metal-catalyzed cross-coupling reactions are one of the most powerful tools in organic synthesis. Palladium and nickel catalysts have been the dominant choice for such a purpose, and are widely used in academia as well as in industry. Whereas iron, a practically ideal transition metal, has been actively investigated as a catalyst in the field of cross-coupling reactions, enyne cross-coupling has remained a challenge because of considerable stability and poor reactivity of alkenyl iron intermediate. We have developed efficient enyne cross-coupling of alkenyl halides and triflates with alkenyl magnesium reagents using lithium bromide as a crucial additive, which would accelerate reductive elimination from alkenyl iron intermediate.

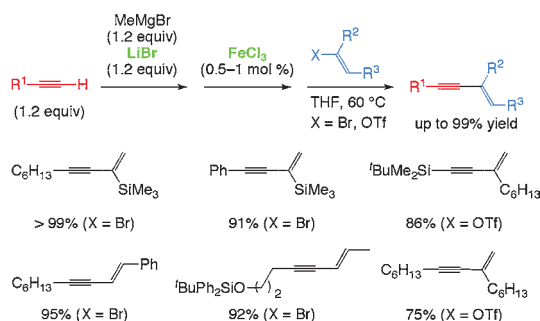


Figure 1. Enyne cross-coupling.

## Cross-Coupling of Alkyl Halides with Alkenylzinc Reagents

Cross-coupling reaction of carbon electrophiles with alkenylmetal reagents is a useful method for olefin synthesis. During the past decade, the scope of the alkenyl coupling has been extended by developing efficient cross-coupling of alkyl halides with alkenylmetal reagents by using copper, palladium, cobalt and iron catalysts. There have been, how-

ever, considerable limitations to be solved (e.g. insufficient yields from secondary alkyl halides, nonavailability of alkyl chlorides). We have developed a powerful protocol for alkyl-alkenyl coupling, which has been accomplished by combination of readily available alkenylzinc reagents, iron pre-catalyst, and TMEDA as an additive. This reaction has several synthetically attractive features: (1) high-yielding, (2) chemoselective, (3) stereospecific, and shows broader substrate scope.

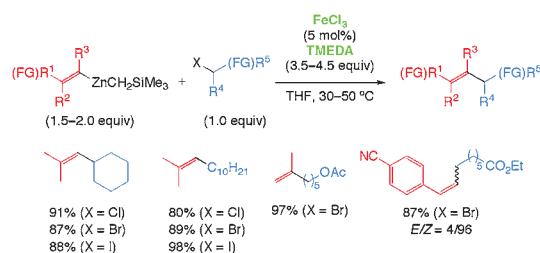


Figure 2. Cross-coupling of alkyl halides with alkenylzinc reagents.

## Programmable Metal Unit Arrangement on Peptides to Create Composition- and Configuration-Controlled Heterometallic Hybrid Materials

The focus of this project is to research the following challenges: i) Development of fundamental method to create composition- and configuration-controlled heterometallic hybrid molecules using metallated-amino acids and peptides as metal units. Programmable metal unit arrangement through chemical synthesis and self-assembly process is employed in complementary to control the composition, 1D/2D array, and 3D configuration of metals on peptides. ii) Screening the function of heterometallic hybrid molecules. Application to supramolecular gelators, molecular electronic devices, photochemical devices, advanced catalysts, artificial enzymes, and MRI contrast agents will be explored with a diverse library of metallated-amino acids and peptides.

Conference on Cutting-Edge Organic Chemistry in Asia under Asian Core Program (ICCEO-3), Hangzhou, China, 19–23 October 2008.

### Grants

Nakamura M, Development of New Synthetic Organic Reactions Based on the Universal Metals Catalysis, Grant-in-Aid for Young Scientists (S), 1 April 2008–31 March 2013.

Nakamura M, Design of Transition Metal/Main Group Elements Synergetic Reagent and Its Synthetic Application, Grant-in-Aid for Scientific Research on Priority Areas, 1 April 2006–31 March 2010.

Takaya H, A New Approach to Chemical Atom Manipulation: Programmable Metal Unit Arrangement on Peptides

to Create Composition- and Configuration-Controlled Heterometallic Hybrid Materials, Precursory Research for Embryonic Science and Technology, 1 April 2006–31 March 2010.

Hatakeyama T, Cross-Coupling Reaction Controlled by Fluoride Ion and Carbene Ligand, Grant-in-Aid for Scientific Research on Priority Areas, 1 April 2008–31 March 2010.

### Award

Takaya H, The Presentation Award for Young Chemists, The 88th Annual Meeting of the Chemical Society Japan, “Programmable Metal Unit Arrangement on Peptides to Create Combination and Configuration-Controlled Organometallic Materials”, Tokyo, 29 March 2008.