

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

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## Visitors

Prof Norbert Krause	Dortmund University, Germany, 17 November 2009
Dr Loic Lemiegre	Ecole Nationale Supérieure de Chimie de Rennes, France, 13 April 2009
Dr Daisuke Hashizume	Riken, Japan, 19 June 2009
Prof Martin Kotora	Charles University, Czech Republic, 10 November 2009
Prof Petr Stepnicka	Dept. of Inorganic Chemistry, Charles University, Czech Republic, 10 November 2009
Prof Milan Pour	Dept. of Pharmacy, Charles University, Czech Republic, 10 November 2009
Dr Jan Vesely	Dept. of Organic Chemistry, Charles University, Czech Republic, 10 November 2009

## 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 2009)

### Publications

Noda D, Sunada Y, Hatakeyama T, Nakamura M, Nagashima H: Effect of TMEDA on Iron-catalyzed Coupling Reactions of ArylMgX with Alkyl Halides, *J. Am. Chem. Soc.*, **131**, 6078-6079 (2009).

Hatakeyama T, Hashimoto S, Ishizuka K, Nakamura M: Highly Selective Biaryl Cross-Coupling Reactions between Aryl Halides and Aryl Grignard Reagents: A New Catalyst Combination of *N*-Heterocyclic Carbenes and Iron Cobalt and Nickel Fluorides, *J. Am. Chem. Soc.*, **131**,

11949-11963 (2009).

Ito S, Fujiwara Y, Nakamura E, Nakamura M: Iron-Catalyzed Cross-Coupling of Alkyl Sulfonates with Aryl-zinc Reagents, *Org. Lett.*, **11**, 4306-4309 (2009).

Hatakeyama T, Nakagawa N, Nakamura M: Iron-Catalyzed Negishi Coupling toward an Effective Olefin Synthesis, *Org. Lett.*, **11**, 4496-4499 (2009).

Hatakeyama T, Kondo Y, Fujiwara Y, Takaya H, Ito S, Nakamura E, Nakamura M: Iron-Catalyzed Fluoroaromatic Coupling Reactions under Catalytic Modulation with 1,2-

## Iron-Group-Metal Fluoride-Catalyzed Biaryl Coupling

Combinations of *N*-heterocyclic carbenes (NHCs) and fluoride salts of the iron-group metals (Fe, Co, and Ni) have been shown to be excellent catalysts for the cross-coupling reactions of aryl Grignard reagents ( $\text{Ar}^1\text{MgBr}$ ) with aryl and heteroaryl halides ( $\text{Ar}^2\text{X}$ ) to give unsymmetrical biaryls ( $\text{Ar}^1\text{-Ar}^2$ ). Based on stoichiometric control experiments and theoretical studies the origin of the unique catalytic effect of the fluoride counterion can be ascribed to the formation of a higher-valent heteroleptic metalate  $[\text{Ar}^1\text{M}^{\text{II}}\text{F}_2]\text{MgBr}$  as the key intermediate which undergoes oxidative addition with  $\text{PhCl}$  and releases the biaryl cross-coupling product  $\text{Ph-Ph}$  with reasonable energy barriers. The present cross-coupling reaction provides a highly selective and practical method for the synthesis of unsymmetrical biaryls as well as the opportunity to gain new mechanistic insights into the metal-catalyzed cross-coupling reactions.

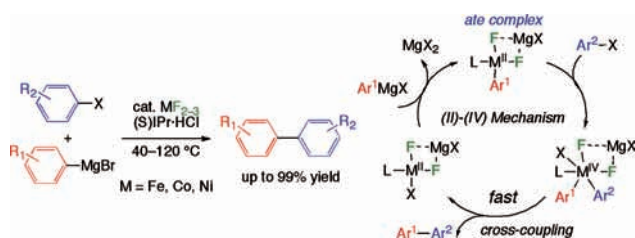


Figure 1. Selective Biaryl Coupling via (II)-(IV) Mechanism.

## Iron-Catalyzed Suzuki-Miyaura Coupling

Recently iron catalysis has been intensively developed in the field of cross-coupling reaction due to its ready availability as well as high catalytic activity for the coupling of secondary alkyl halides very often superior to those of the conventional palladium and nickel catalysts. However Suzuki-Miyaura coupling among the most practical cross-coupling reaction has not been established well. We found lithium arylborate **1** prepared from arylboronic acid pinacol ester and alkyllithium can effectively cross-coupled with alkyl halides in the presence of catalytic

amount of iron (II) chloride-bisphosphine complex **2** and magnesium bromide. The features of the present method are: high-yielding chemoselective and free of rare metals showing its potential in efficient and versatile access to functional aromatic compounds.

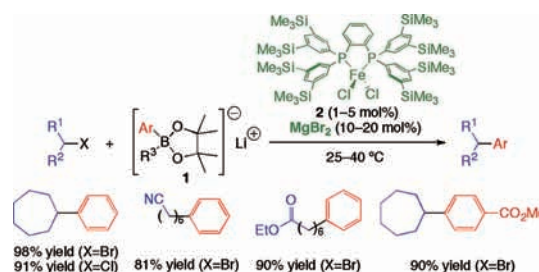


Figure 2. Suzuki-Miyaura Coupling of Alkyl Halides with Arylborates.

## 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 photochemical devices advanced catalysts artificial enzymes and MRI contrast agents will be explored with a diverse library of metallated-amino acids and peptides.

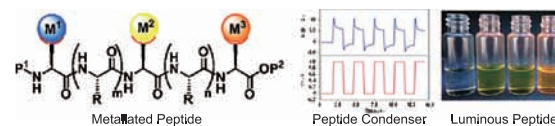


Figure 3. Preparation of Metallated Peptide and Self-Assembly of the Peptide.

Bis(diphenylphosphino)benzene, *Chem. Commun.*, 1216-1218 (2009).

## Presentations

Selective Cross-Coupling Reactions Based on Iron Catalyst, Nakamura M, Summer Symposium The Japanese Society for Process Chemistry, 16-17 July 2009, Chiba, Japan (invited).

Iron-Catalyzed Suzuki-Miyaura Coupling Reaction, Nakamura M, The 14th Japan-Korea Symposium on Organic Chemistry, 23-26 October 2009, Atami, Japan (invited).

Selective Cross-Coupling Reactions Based on Iron and Iron-Group Metal Catalysts, Nakamura M, Japan Petroleum Institute Catalyst Symposium, 24 November 2009, Tokyo, Japan (invited).