

Young Career Focus: Professor Takanori Iwasaki (The University of Tokyo, Japan)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents Professor Takanori Iwasaki (The University of Tokyo, Japan).

Biographical Sketch



Prof. T. Iwasaki

Takanori Iwasaki was born and raised in Osaka, in the southern-central region of Japan. He finished his BSc in 2004 and MSc in 2006 at the Graduate School of Engineering Science, Osaka University (Japan), and received his PhD in 2009 from the same university under the supervision of Professors Kazushi Mashima and Takashi Ohshima, where he worked on the zinc-cluster-catalyzed transformations of esters. During his PhD course, he worked with Professor Karl Kirchner, Vienna University of Technology (Austria) in 2004. He became an Assistant Professor at the Graduate School of Engineering, Osaka University in 2009, working with Professor Nobuaki Kambe, and was promoted to Associate Professor in 2017, where he developed late-transition-metal-catalyzed cross- and multicomponent coupling reactions. In the summer of 2018, he was appointed Associate Professor at The University of Tokyo (Japan). He received the Japan Society for Process Chemistry (JSPC) Award for Excellence 2008, Asahi Kasei Pharma Award in Synthetic Organic Chemistry, Japan in 2011, The Ube Foundation Young Researcher Award in 2014, Special Lecture for Young Chemists in 96th the Chemical Society of Japan (CSJ) in 2016, CSJ Presentation Award 2017, Chemistry Award BCA 2018, Incentive Award in Synthetic Organic Chemistry, Japan in 2018, Thieme Chemistry Journals Award 2019, and The Japan Petroleum Institute Award for Encouragement of Research and Development in 2019. He was also selected as finalist of Reaxys PhD Prize 2010. His research interests include the development of multi-metallic catalytic systems for the cooperative activation of substrates toward challenging transformations.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Prof. T. Iwasaki My major research interest is the development of catalytic systems, which consist of multiple metal centers, and their application to challenging transformations.

Organic synthesis can create new molecules by repeating bond cleavage and formation. Organic chemists often use highly active reagents for bond cleavage and formation to activate one of the substrates. In this case, the counterpart reacts with the activated substrate based on its own reactivity. When the reaction is applied to multi-functionalized compounds, the chemoselectivity is difficult to control in many cases. To overcome this issue, I focus on the simultaneous activation of both substrates by catalysts to achieve the catalyst-controlled chemoselectivity.

In particular, I am interested in multinuclear metal complexes as catalysts and have achieved chemoselective reactions, such as *O*-selective acylation of amino alcohols, selective cleavage of the carbon–fluorine bond in the presence of more reactive chemical bonds, and so on. In addition, I have demonstrated that the simultaneous activation of two substrates on multinuclear metal complexes kinetically accelerates reactions to allow the use of less reactive chemical bonds as reacting sites.

SYNFORM *When did you get interested in synthesis?*

Prof. T. Iwasaki I started my research activities at Osaka University, where I tried to synthesize a new bimetallic complex supported by a novel multidentate ligand. The synthesis of the new multidentate ligand resulted in a litany of failures because of hidden pitfalls in the synthesis, such as lower efficiency of the reported reaction conditions for my target molecule and facile decomposition of molecules during

multistep manipulations. Eventually, I succeeded in synthesizing the ligand using a catalyst I newly developed myself. During the ligand synthesis, I was fascinated by synthetic organic chemistry using catalysis.

SYNFORM *What do you think about the modern role and prospects of organic synthesis?*

Prof. T. Iwasaki I believe that organic synthesis will retain its standing at the center of mainstream science and will continue to contribute to the progress of humankind through the supply of materials. Synthetic organic chemistry has developed much over the last 100 years. In my opinion, the advancement of analytical technology as well as catalyst technology represented by transition-metal catalyses has contributed greatly to the progress of organic chemistry. This progress will continue or even accelerate with the aid of these technologies, along with leading-edge informatics and automation technologies, to bring organic synthesis to a level unimaginable today. Although it is concerning that the rise of informatics and automation technologies will eliminate the need for organic synthetic chemists from both industry and academic positions, I am not so pessimistic over the future of organic synthetic chemists. Looking back on history, new technologies freed organic synthetic chemists from complicated manipulations and gave them time to focus on more creative works. I envisage a future where we can concentrate more on creative works and can try our own ideas easily using these new technologies. As a conclusion, I am confident that synthetic organic chemistry will continue to develop as a discipline that creates new molecules.

SYNFORM *Could you tell us more about your group's areas of research and your aims?*

Prof. T. Iwasaki For now, my group is focusing on rational design of metal complexes, which have two catalytically active sites. An important concept for me is connecting these two functions flexibly. Although there are many reports on multi-functional catalysts, these catalytic sites are often connected by a rigid backbone of ligands to fix the relative positions of these catalytic sites. This may cause difficulty in the catalyst design and synthesis of supporting ligands. In my concept, electrostatic interaction between ion pairs of an ionic transition-metal complex is used as a flexible connection of two catalytic active sites. For example, ate complexes generated by the reaction of neutral transition-metal complexes with appropriate organometallic reagents such as Grignard reagents were employed for the C–C bond-forming reactions

as catalysts. In particular, the cross-coupling reaction of alkyl halides with tertiary alkyl Grignard reagents to construct quaternary carbon center was catalyzed by cobaltate complex **1** (Figure 1). It should be noted that alkyl fluorides could be used as a coupling partner in the Co-catalyzed cross-coupling reaction, and the C–F bond, which is the strongest single bond in organic compounds, was smoothly cleaved even under mild conditions. The unexpectedly facile cleavage of the C–F bond is due to its cooperative activation by the Lewis acidic counter cation in cobaltate complex **1**. Because alkyl fluorides are inert toward conventional catalyses and reagents, late-stage construction of a quaternary carbon center via the cross-coupling reaction was successfully demonstrated. Anionic Fe complex **2** bearing cyclopentadienyl ligand was found to catalyze a similar cross-coupling reaction.

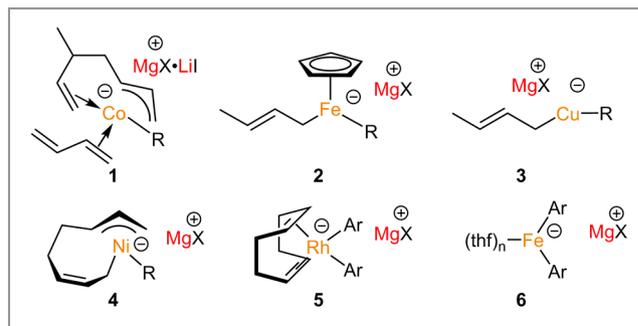


Figure 1 Structure of transition-metal ate complexes

Other examples of the use of alkyl fluorides as alkylating reagents are Cu-catalyzed internal-carbon-selective reductive alkylation of 1,3-dienes and Ni-catalyzed dimerization and alkylation of 1,3-dienes promoted by anionic allyl-metal intermediates **3** and **4**, respectively. In these reactions, alkyl fluorides are the best alkylating reagents, and other alkyl halides led to poor results.

The concept of ate-complex-mediated activation of less reactive chemical bonds could be expanded to the cross-coupling reaction of vinylic ethers with aryl Grignard reagents via C–O bond cleavage catalyzed by anionic diarylrhodate **5** and related Fe complex **6**.

SYNFORM *What is your most important scientific achievement to date and why?*

Prof. T. Iwasaki My most important scientific achievement, I think, is the demonstration of the cooperative activation of alkyl electrophile and carbon nucleophile by ate complexes. As briefly mentioned above, I found Ni-catalyzed

four-component-coupling reaction of alkyl fluorides, aryl Grignard reagents, and two molecules of 1,3-butadiene. From exhaustive mechanistic studies and theoretical calculations on the reaction, I determined the reaction mechanism as follows: (1) actual catalytic species at the C–F bond-cleavage step are nickelate complex **4**, generated by the reaction of Ni(0) with two molecules of 1,3-butadiene and subsequent complexation with Grignard reagent, (2) entropy does not contribute to the C–F bond-cleavage step, and (3) the magnesium cation of nickelate coordinates to the fluorine atom, and the anionic nickel approaches from the opposite side at the transition-state-determined theoretical calculations. These observations clearly support my concept of cooperative activation of both nucleophile and electrophile on each metal center of the ate complex. I hope that the insight of the chemistry of ate complexes provides useful information for designing catalytic intermediates in organometallic and synthetic organic chemistry.

Mattias Forsell