Reaction Scope and Mechanistic Insights of Nickel-Catalyzed Migratory Suzuki–Miyaura Cross-Coupling

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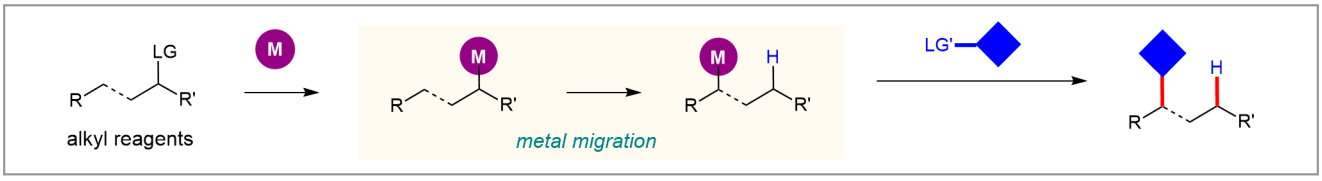
Metal-catalyzed cross-coupling reactions have revolutionized carbon–carbon bond disconnections in synthetic chemistry. In this context, β-hydrogen-containing sp^3-carbon electrophiles are generally recognized to be more challenging than their sp^2-carbon analogues owing to the possibility of β-hydride elimination taking place as side reaction. During the past several decades, extensive efforts have been devoted to avoiding β-hydride elimination and constructing chemical bonds at the sp^3-carbon through metal-catalyzed cross-coupling. Recently, migratory cross-coupling reactions have been emerging as a new research field, as these reactions allow the generation of products through an iterative migratory insertion/β-H elimination process (Scheme 1). The net result of this process is the controlled functionalization of a carbon atom different from the one originally carrying the metal.

Since the group of Professor Yin (Wuhan University, P. R. of China) began their research in this field in 2017, they have been committed to expanding the scope of migratory cross-coupling reactions and have conducted an in-depth study on the mechanism of these reactions. The migratory Suzuki–Miyaura cross-coupling represents the latest progress of the Yin group in this field. Electrophilic alkyl reagents (including alkyl chlorides, bromides, iodides and tosylates) have given satisfactory results (Figure 1a) when engaged in the reaction.



Scheme 1 Nickel-catalyzed migratory cross-coupling

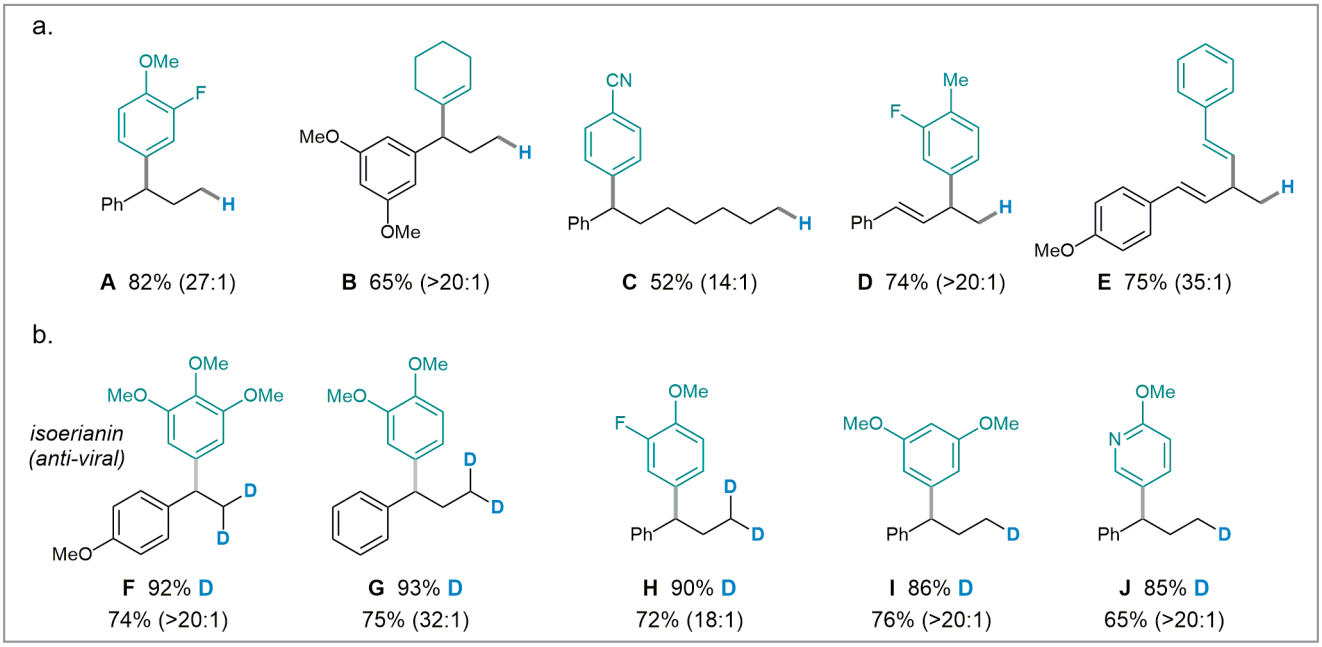


Figure 1 Scope of the reaction

Professor Yin explained: "Our method offers a protocol to rapidly access diarylalkanes and allylbenzenes from a series of aryl/vinyl-bearing alkyl electrophiles and sp^2-C boron-based nucleophiles. This approach is characterized by a broad substrate scope and excellent migratory regioselectivity. Interestingly, this strategy can serve as a platform for the synthesis of terminal, partially deuterium-labeled molecules from readily accessible starting materials (Figure 1b). These kinds of compounds are difficult to obtain by common synthetic methods."

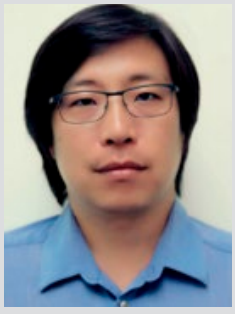
Professor Yin's group has studied the reaction mechanism by a combination of experimentation and calculation. Experimental studies suggest that migratory cross-coupling products are generated from a Ni(0/II) catalytic cycle. Theoretical calculations indicate that the chain-walking occurs at a neutral nickel complex rather than at a cationic one. Interestingly, Professor Yin and co-workers found that the classical Suzuki–Miyaura coupling reaction and the migratory Suzuki–Miyaura coupling reaction proceed through distinctly different pathways. "We believe that the study of the reaction mechanism will help us in understanding the reaction process and is of great significance to further expanding the scope of this particular migration reaction," remarked the authors.

Professor Yin concluded by mentioning some future prospects: "Our research group will continue to carry out research in this field and develop more practical synthesis methods."

About the authors

Prof. G. Yin

Prof. Guoyin Yin received his Ph.D. from Shanghai Institute of Organic Chemistry (SIOC), Chinese Academy of Sciences (CAS, P. R. of China) in 2011, under the supervision of Prof. Guosheng Liu. Starting in late 2011, he conducted postdoctoral research at Technical University of Munich (Germany) with Prof. Thorsten Bach as an Alexander von Humboldt Postdoctoral Fellow, at RWTH Aachen University (Germany) with Prof. Franziska Schoenebeck, and at the University of Delaware (USA) with Prof. Donald A. Watson. In 2016, he began his independent career at the Institute for Advanced Studies (IAS) of Wuhan University (P. R. of China). His research interest currently focuses on transformations involving metal migration.



Prof. Y. Lan

Prof. Y. Lan completed his Ph.D. in 2008 at Peking University (P. R. of China) under the supervision of Professor Yun-Dong Wu. From 2009 to 2012, he worked as a postdoctoral fellow at the University of California, Los Angeles (USA) with Professor K. N. Houk. He then joined the faculty of Chongqing University (P. R. of China). In 2016, he received the Chinese Chemical Society Award for Outstanding Young Chemist. His current research interest focuses on the mechanism and selectivity of transition-metal-mediated coupling reactions with DFT calculations.

Y. Li

Yuqiang Li was born in Anhui Province (P. R. of China) and received his B.Sc. degree from Central South University in 2016. Subsequently, he pursued his Ph.D. under the guidance of Prof. Guoyin Yin at Wuhan University (P. R. of China). His research topic focuses on cross-coupling reactions involving metal migration.

Y. Luo

Yixin Luo received her BS degree at Chongqing Normal University (P. R. of China) in 2016. Currently, she is pursuing her PhD under the supervision of Prof. Yu Lan at Chongqing University. Her current research interests are focused on the mechanistic study of transition-metal-catalyzed cross-coupling reactions.

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