Mechanistic Studies on Palladium-Catalyzed Regioselective and Stereospecific Aziridine Ring-Opening Cross-Coupling Reactions

W. M. C. Sameera, Youhei Takeda, Satoshi Minakata, Keiji Morokuma

1Department of Chemistry, Faculty of Science, Hokkaido University, Kita-Ku, Sapporo, 060-0810, Japan.
2Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamadaoka 2-1, Suita, Osaka 565-0871, Japan.
3Fukui Institute for Fundamental Chemistry, Kyoto University, Takano-Nishihiraki-cho 34-4, Sakyo-ku, Kyoto 606-8103, Japan.

*E-mail: wmcsameera@sci.hokudai.ac.jp

Transition metal catalysis is an efficient way to perform catalytic reactions in a controlled and a selective fashion. Quantitative details of mechanisms and selectivity of catalytic reactions are very important for the development of new and/or more efficient catalytic reactions. However, these properties are difficult to characterize only from experimental studies. Recent advances in the density functional theory and density functional theory molecular mechanics mean that complex catalytic reactions can now be determined more accurately [1–3]. Herein we present our recent mechanistic studies on palladium-catalyzed regioselective and stereospecific aziridine ring-opening reactions.

We have recently developed the first example of catalytic borylative ring-opening of nonvinylclic aziridines (Fig. 1) [4]. The computed catalytic cycle consists of the oxidative addition of aziridine to Pd(0), rate-determining proton transfer, a phosphine ligand dissociation from the catalyst, transmetalation, cis/trans isomerization, and reductive elimination. The regioselectivity-determining aziridine ring-opening step proceeds at the terminal carbon in an S₂ fashion. Calculated regioselectivity is in good agreement with the experimental data.

Also, we have reported a Pd-catalyzed regioselective and enantiospecific cross-coupling reaction of 2-aryl-substituted aziridines with arylboronic acids to give biologically important 2-arylphenethylamine derivatives (Fig. 2) [5]. In this reaction, aziridine ring opening occurs at the benzylic carbon (the 2nd position) of aziridine substrate, where the opposite regioselectivity of the ring opening to that observed in borylative substrate, where the opposite regioselectivity of the ring opening reaction (Fig. 1) was achieved. Our computational studies rationalize the mechanism and regioselectivity of this reaction.

![Fig.1 Borylative ring-opening of nonvinylclic aziridines.](image1)

![Fig.2 Cross-coupling reaction of 2-aryl-substituted aziridines with arylboronic acids.](image2)

REFERENCES