

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

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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 nonvinylic 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 S_N2 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 regioselection of the ring opening to that observed in borylative ring opening reaction (Fig. 1) was achieved. Our computational studies rationalize the mechanism and regioselectivity of this reaction.

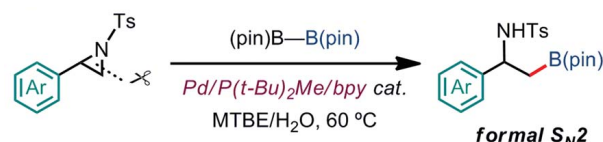


Fig.1 Borylative ring-opening of nonvinylic aziridines.

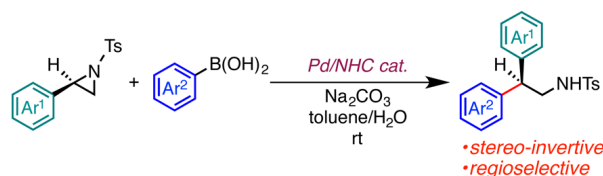


Fig.2 Cross-coupling reaction of 2-aryl-substituted aziridines with arylboronic acids.

Our experimental and computational studies offer important mechanistic insights to develop broadly applicable catalysts for aziridine ring-opening reactions potential applications in industry and academia.

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