Over the last few decades, the quest for environmentally benign chemical transformations has become an important topic in both industrial and academic research. Thus, in order to develop highly atom-economical and environmentally benign synthetic processes, we have focused on the development of highly selective and practical direct catalytic reactions.

In this lecture, I will present two newly developed catalyses for the synthesis of unnatural α-amino acid derivatives; (1) α-amination of carboxylic acid derivatives and (2) nucleophilic addition to N-unprotected α-ketiminnoesters.

(1) α-amination of carboxylic acid derivative is regarded as one of the most straightforward methods for the synthesis of unnatural α-amino acids. While several elegant α-amination reactions have been developed, only limited examples using carboxylic oxidation state substrates were reported and the use of more than stoichiometric amount of strong base is usually inevitable. Recently, we developed a catalytic α-amination under mild conditions using acylpyrazole as a pre-nucleophile. Under the optimized conditions using Cu(OTf)$_2$, α-amination reactions proceeded efficiently with wide functional group tolerance. Notably, the bidentate coordination mode of acylpyrazoles was amenable to highly chemoselective activation over ketone and much more acidic nitroalkyl functionality.

(2) Nucleophilic addition to ketimines is also one of the most straightforward approaches to synthesize optically active tetrasubstituted amines. Recently, several direct catalytic additions to N-protected ketimines were reported including our Rh-catalysis. To obtain N-unprotected amines, however, they require additional deprotection steps, which limit their synthetic utilities. A prominent way to address these issues is using N-unprotected ketimines; however, there are only limited success using N-unprotected ketimines as an electrophile. Recently, we succeeded in the development of Zn-catalyzed direct asymmetric addition of terminal alkynes and 1,3-dicarbonyl compounds, to N-unprotected ketimines. Very surprisingly, Zn-catalyzed alkynylation selectively proceeded with N-unprotected ketimines over the N-PMP-protected ketimines and aldines. Moreover, we also developed direct catalytic Mannich-type reactions to N-unprotected ketiminoesters for direct access to N-unprotected α- and/or β-tetrasubstituted amino acid esters.