Modularly Designed Supramolecular Catalytic Assembly for the Strategic Enantioselective Borylation of Remote C–H Bonds

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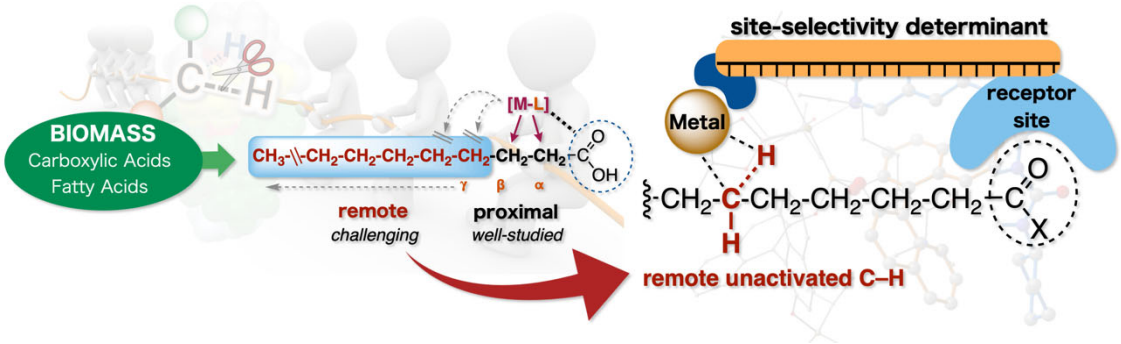
ABSTRACT

There exists in nature efficient catalytic systems that enable the challenging functionalization of ubiquitous C–H bonds in diverse substrate classes. Enzymatic assemblies have inspired the creation of wide-ranging synthetic supramolecular catalysts that mimic their proficient activities. Despite the conceptual advances of these synthetic biomimetic systems, the elaborate preparations and limited substrate compatibility limit their utilities in organic synthesis.

With our interest in the development of novel methodologies for the transformation of C–H bonds in readily available feedstock chemicals, we previously demonstrated the competent activation and subsequent asymmetric borylation of C(sp^3)–H bonds under Ir or Rh catalysts utilizing a chiral monophosphite ligand system allowing the preparation of biologically-active and synthetically useful organoboronates.[1,2] Our collaboration with ICReDD scientists has given us infinite opportunity to further extend the reactivity of our catalytic system. Thus, guided by calculation derived transition-state models, we recently succeeded in the asymmetric borylation of remote γ-C–H bonds in aliphatic carboxylic amides and esters using a chiral, modular Ir-monophosphite catalyst and a urea receptor ligand that recruits the substrate via noncovalent interactions – a direct functionalization realized using a modularly designed supramolecular catalytic assembly.[3] In this aspect, the overall efficiency relies on the crucial interactions between the catalytic system and the substrate within a reaction cavity or pocket that resembles the active site of natural enzymes. Inspired and goal-driven by these results, further collaboration and joint efforts has led us to the possibility of designing catalytic assemblies to target more distal C–H bonds in the aliphatic hydrocarbon chain of common and readily available chemical feedstocks including biomass resources allowing for a more sustainable and efficient organic synthesis.

In this presentation, the development of catalytic enantioselective borylation of C–H bonds will be described in the context of reaction discovery, design, and utility. Strategic convergence of experimental and theoretical studies will be outlined to emphasize our approach in targeting remote C–H bonds beyond the γ-position, further highlighting the need for the creation of methodologies that will allow challenging transformations.



REFERENCES

1. R. L. Reyes, T. Iwai, S. Maeda, M. Sawamura, Iridium-catalyzed Asymmetric Borylation of Unactivated Methylene C(sp^3)–H Bonds. *J. Am. Chem. Soc.* **2019**, *141*, 6817–6821.
2. R. L. Reyes, M. Sato, T. Iwai, M. Sawamura, Asymmetric Synthesis of α-Aminoboronates via

Rhodium-Catalyzed Enantioselective C(sp^3)–H Borylation. *J. Am. Chem. Soc.* **2020**, *142*, 589–597.
3. R. L. Reyes, M. Sato, T. Iwai, K. Suzuki, S. Maeda, M. Sawamura, Asymmetric Remote C–H Borylation of Aliphatic Amides and Esters with a Modular Iridium Catalyst. *Science* **2020**, *369*, 970–974.