Asymmetric Remote C–H Bond Borylation with a Modular Iridium Catalyst

(*[1]Department of Chemistry, Faculty of Science, Hokkaido University, [2]Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Sapporo, Japan)*
○ Ronald L. Reyes,[1,2] Miyu Sato,[1] Tomohiro Iwai,[1] Kimichi Suzuki,[2] Satoshi Maeda,[1,2] Masaya Sawamura[1,2]
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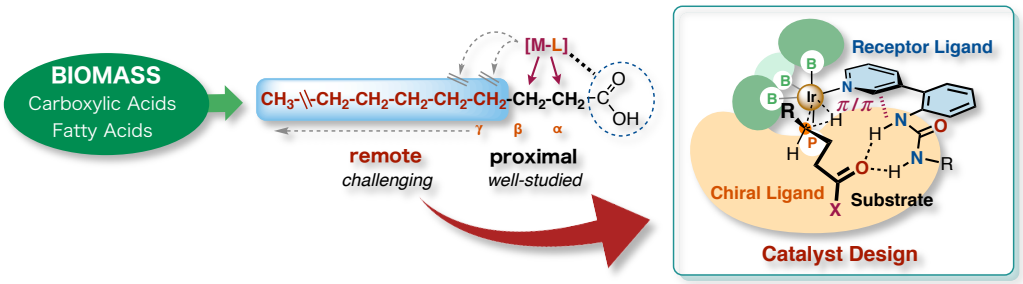
The direct functionalization of C–H bonds has emerged as an attractive and powerful tool to introduce molecular complexity.[1] In particular, the prevalence of aliphatic carboxylic acids and their derivatives as common feedstock chemicals has resulted to the upsurge of methodologies for the direct activation of C–H bonds within their hydrocarbon framework. However, compared to the functionalization of proximal C–H bonds, remote C(sp^3)–H bonds in these compounds is far less developed.

Here we report a highly enantio- and site-selective catalytic borylation of remote C(sp^3)–H bonds γ to the carbonyl group in aliphatic carboxylic acid derivatives.[2] A high-performing chiral C–H activation catalyst was modularly assembled from an iridium center, a chiral monophosphite ligand, an achiral urea-pyridine receptor ligand, and pinacolatoboryl groups. Quantum chemical calculations support an enzyme-like structural cavity formed by the catalyst components, which bind the substrate through multiple noncovalent interactions. Versatile synthetic utility of the enantioenriched γ-borylcarboxylic acid derivatives was demonstrated paving the opportunity for developing strategic synthetic tools for building structural diversity from readily available raw materials.



1) a) T. G. Saint-Denis, R.-Y. Zhu, G. Chen, Q.-F. Wu, J.-Q. Yu, *Science* **2018**, *359*, eaao4798. b) C. G. Newton, S.-G. Wang, C. C. Oliveira, N. Cramer, *Chem. Rev.* **2017**,*117*, 8908–8976.
2) R. L. Reyes, M. Sato, T. Iwai, K. Suzuki, S. Maeda, M. Sawamura, *Science* **2020**, *369*, 970–974. For our recent works on C(sp^3)–H functionalization see: *J. Am. Chem. Soc.* **2019**, 141, 6817–6821; *J. Am. Chem. Soc.* **2020**, *142*, 589–597.