



## Catalytic Enantioselective Borylation of Methylene C–H Bonds

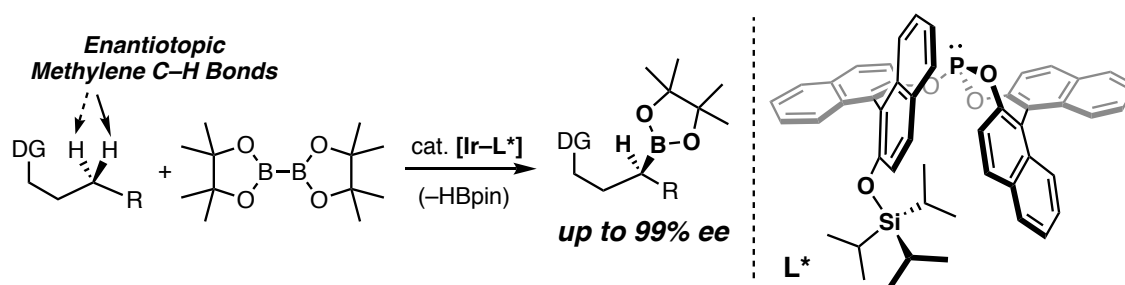
Ronald L. Reyes,<sup>1,2</sup> Tomohiro Iwai,<sup>1</sup> Satoshi Maeda,<sup>1,2</sup> and Masaya Sawamura<sup>1,2</sup>

<sup>1</sup>Department of Chemistry, Faculty of Science, Hokkaido University;

<sup>2</sup>Institute for Chemical Reaction Design and Discovery, Hokkaido University)

Transformative synthetic strategies that circumvent challenges in the activation of C(sp<sup>3</sup>)–H bonds remain unprogressive despite the significant advances in catalytic C–H functionalization. Proven crucial to this endeavor is the construction of suitable catalytic systems that can facilitate the differentiation of C(sp<sup>3</sup>)–H bonds. Our group previously described a heteroatom-directed borylation of C(sp<sup>3</sup>)–H bonds with Rh- or Ir-catalyst systems based on immobilized, silica-supported bridgehead monophosphine, such as Silica-SMAP and Silica-TRIP, allowing the site-selective borylation of the *N*-adjacent or unactivated C(sp<sup>3</sup>)–H bonds located  $\gamma$  to *N* or *O* atoms on the directing groups.<sup>1,2</sup> We have also recently disclosed the development of an asymmetric C(sp<sup>3</sup>)–H borylation using a chiral BINOL-based phosphoramidite as a ligand providing secondary alkylboronates with moderate levels of enantioselectivity.<sup>3</sup>

Realizing the importance of stereochemistry-generating C–H activation approaches, in this presentation, we report the development of an innovative chiral catalyst system enabling the asymmetric differentiation of enantiotopic methylene C(sp<sup>3</sup>)–H bonds. Accordingly, the iridium-catalyzed asymmetric borylation of internal methylene C–H bonds in 2-alkylpyridine and 2-alkyl-1,3-azole derivatives proceeded with excellent enantioselectivity. Computational studies using the artificial force induced reaction (AFIR) method suggested the importance of the overall conformational effect featuring a trisboryliridium(III) species that allows the creation of a chiral reaction pocket for substrate accommodation along with crucial secondary interactions arising from  $\pi$ -stacking, CH– $\pi$ , and C–H $\cdots$ O noncovalent bonding between the substrate and the catalyst.



### < REFERENCES >

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Name Ronald L. Reyes  
 Affiliation Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University  
 Position Post-doctoral Researcher (PD)  
 Group Organometallic Chem. Lab. (Sawamura Group)

