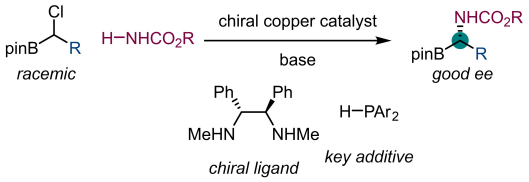
Enantioselective Synthesis of α-Aminoboronic Acid Derivatives via Copper-Catalyzed N-Alkylation

G. Zuccarello[1], S. M. Batiste[1], H. Cho[1], G. C. Fu[1]*

[1]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

Optically active α-aminoboronic acids, bioisosteres of natural α-amino acids, find application in medicinal chemistry as antitumor, antiviral, and antibacterial agents and for the treatment of type II diabetes. Herein, we present a new direct synthetic strategy based on the enantioselective cross-coupling of readily available racemic α-chloro boronates with carbamates using an earth-abundant copper catalyst with commercial DMPEDA and a diaryl phosphine as the ligands. These reaction conditions originated from a detailed mechanistic study of a photoinduced system.



reaction development: driven by mechanistic studies

[1] Giuseppe Zuccarello, Suzanne M. Batiste, Hyungdo Cho, Gregory C. Fu *J. Am Chem. Soc.,* **2023**, *145*, 3330–3334.
[2] Guilherme Felipe Sandos Fernandes, William Alexander Denny, Jean Leandro Ds Santos *Eur. J. Med. Chem.* **2019**, *179*, 791–804.
[3] Gregory C. Fu *ACS Cent. Sci.* **2017**, *3*, 692–700.
[4] Caiyou Chen, Jonas C. Peters, Gregory C. Fu *Nature* **2021**, *596*, 250–256.
[5] Hyungdo Cho, Hidehiro Suematsu, Paul H. Oyala, Jonas C. Peters, Gregory C. Fu *J. Am. Chem. Soc.* **2022**, *144*, 4550–4558.