

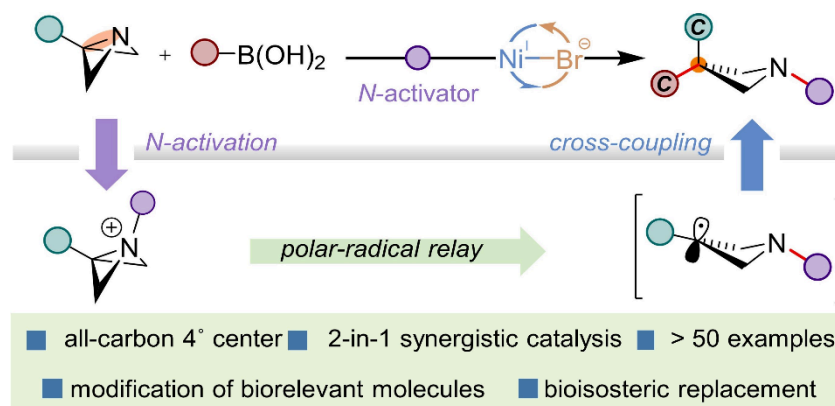
Azetidines with All-Carbon Quaternary Centers: Merging Relay Catalysis with Strain Release Functionalization

Hsuan-Hung Liao

Department of Chemistry, National Sun Yat-sen University, Taiwan, 80424

E-mail: hsuan-hung.liao@mail.nsysu.edu.tw

Given the importance and the beneficial characteristics of decorated azetidines in medicinal chemistry, efficient strategies for their synthesis are highly sought after. My group reports a facile synthesis of the elusive all-carbon quaternary center-bearing azetidines.¹ By adopting a well-designed polar-radical relay strategy, we harness the release of ring strain from bench-stable benzoylelated 1-azabicyclo[1.1.0]butane (ABB) for nickel-catalyzed Suzuki $\text{Csp}^3\text{--Csp}^2$ cross-coupling. This involves the ring-opening of ABB facilitated by synergistic bromide and nickel catalysts derived from a sole nickel source (NiBr_2), leading to ABB's conversion into a redox-active species that subsequently engages in cross-coupling through a radical pathway. Late-stage functionalization of natural products, biologically relevant molecules, and pharmaceuticals have been successfully achieved, as well as the synthesis of melanocortin-1 receptor (MC-1R) agonist and vesicular acetylcholine transporter (VACHT) inhibitor analogs through bioisosteric replacements of piperidine with azetidine moieties, highlighting the potential of the method in drug optimization studies.



Reference

1. Hsu, C. -M.; Lin, H. -B.; Hou, X. -Z.; R. V. P. P. Tapalesa; Shih, C.-K.; S. Miñoza; Tsai, Y.-S.; Tsai, Z.-N.; Chan, C. -L.; Liao, H. -H. *J. Am. Chem. Soc.* **2023**, 145, 34, 19049-19059.



Hsuan-Huang Liao (廖軒宏)

National Tsing Hua University, Taiwan (B.Sc. 2008)

National Tsing Hua University, Taiwan (M.Sc. 2010)

RWTH Aachen University, Germany (Ph.D. 2016)

Postdoctoral Researcher, RWTH Aachen University, Germany
(2016-2017)

Marie Skłodowska-Curie Individual Fellow, University of Bristol, UK
(2017-2019)

Assistant Professor, National Sun Yat-sen University, Taiwan
(2019-2022)

Associate Professor, National Sun Yat-sen University, Taiwan
(2023-present)

[Field of research] Organic Synthesis and Catalysis