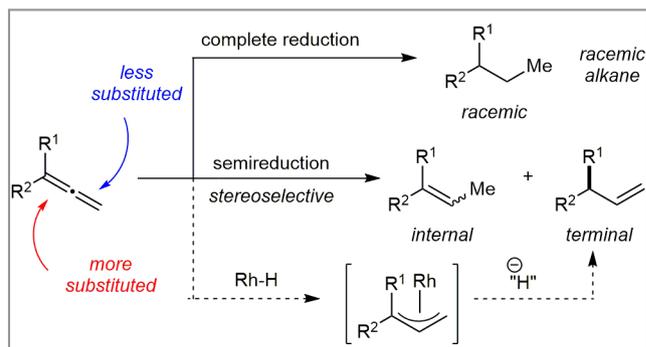


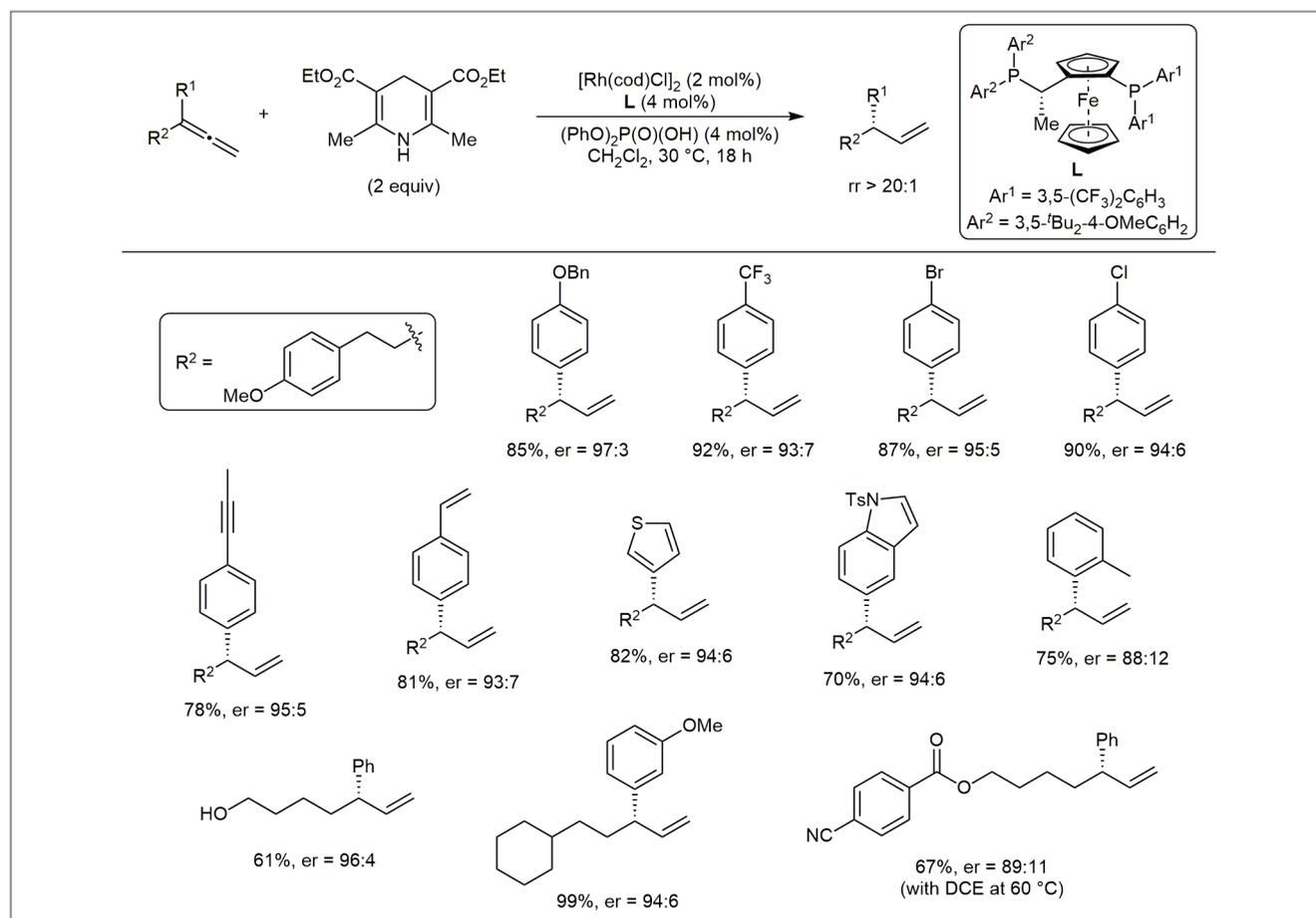
Enantioselective Semireduction of Allenes

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Despite the numerous catalysts and reagents available for the reduction of a wide range of diverse functional groups, the selective reduction of allenes to terminal alkenes remains an unsolved challenge in organic synthesis. In fact, the few existing methods favor the formation of internal olefins. The group of Professor Vy M. Dong at the University of California, Irvine (USA) envisioned that a rhodium-hydride catalyst with a hydride nucleophile could give rise to an asymmetric allene semireduction, which could then lead to products bearing benzylic stereocenters that are common in medicinal chemistry. "It is known that Rh hydrides can insert into allenes to generate Rh-allyl intermediates," explained Professor Dong. She continued: "These species react with various nucleophiles



Scheme 1 Selectivity challenges in allene reduction and proposed method



Scheme 2 Selected substrate scope

to give branched products. In our semi-reduction, the nucleophile is a hydride. Nucleophilic hydride sources have been used in allylic substitutions with allylic electrophiles. Based on literature precedents demonstrating the feasibility of both steps, we were encouraged that our idea would also be feasible.”

The co-author of this *Nature Communications* paper, PhD student Zhiwei Chen, said: “We examined various hydride sources but found that a Hantzsch ester, synthetic analogue of NADH, afforded the highest regioselectivity. Other hydride sources, such as formic acid and silanes, are typically used in allylic substitutions.”

Professor Dong took up the story again: “Next, we found that a designer Josiphos ligand gave the products with excellent regioselectivities and high enantioselectivities without any isomerization of the allenes to the corresponding dienes. Lastly, our allene semi-reduction occurs chemoselectively in the presence of other functional groups, which could undergo reduction under typical hydrogenation conditions. Allenes bearing aryl halides, alkenes, alkynes, nitriles, and esters were selectively semi-reduced to the terminal alkenes.”

Professor Dong concluded: “Although this work represents a major advance in allene semi-reduction, the scope is currently limited to alkyl-aryl-disubstituted allenes. Future work will focus on expanding this method to include other allenes.”

Mattes Fank

About the authors



Z. Chen

Zhiwei Chen was born in Fujian province (P. R. of China) and grew up in Flushing, NY (USA). He obtained his bachelor's degree in chemistry from Queens College of CUNY (USA) in 2014 where he did undergraduate research with Yu Chen. He is currently a Ph.D. candidate in Vy Dong's group at the University of California, Irvine (USA). His research focuses on developing new Rh-catalyzed reactions.



V. M. Dong

Vy Dong was born in Big Spring, Texas (USA) and spent her early childhood in west Texas before moving with the family to Anaheim, California (USA). She graduated magna cum laude from UC Irvine (USA) where she majored in chemistry and completed an honor's project with Larry Overman. After graduation, she joined David MacMillan's group at UC Berkeley (USA), and then moved with his group to Caltech to complete her doctoral studies. Her Ph.D. thesis featured variants of the zwitterionic-Claisen rearrangement and a total synthesis of erythronolide B. As an NIH postdoctoral fellow, Vy pursued training in organometallic and supramolecular chemistry with Robert Bergman and Kenneth Raymond at Berkeley. She began her independent academic career at the University of Toronto (Canada), where she was promoted with tenure and named the Adrian Brook Professor. After six years in Canada, Vy returned to the USA to assume a professorship at her alma mater, UC Irvine. Professor Dong's research team is interested in new reaction methods, enantioselective catalysis, and natural product synthesis.