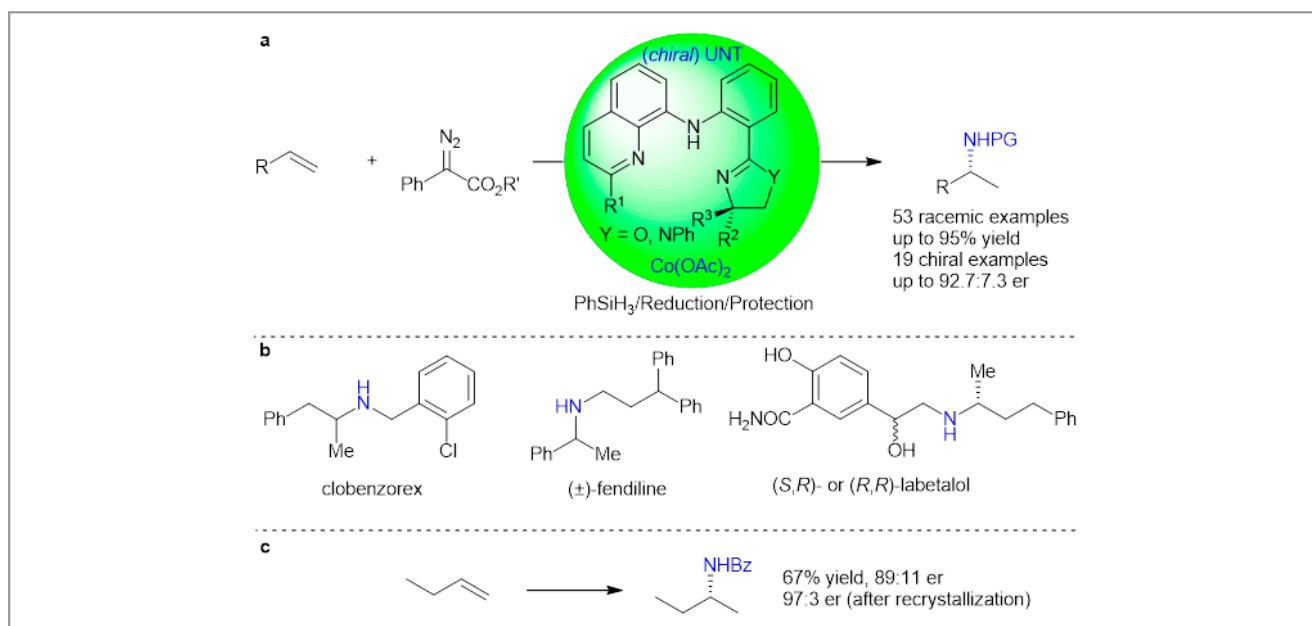


# Ligand-Promoted Cobalt-Catalyzed Radical Hydroamination of Alkenes

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Amines and their derivatives are ubiquitous compounds of great value and paramount importance in a number of areas, including agrochemicals, pharmaceuticals and materials. The development of highly efficient and selective methods to introduce amine groups into organic molecules remains therefore a vibrant area of research in organic synthesis. Since the carbon–carbon double bond is one of the most common structural motifs in organic molecules, highly regio- and enantioselective intermolecular hydroamination of alkenes seems an ideal strategy to access chiral amines. “Probably the most important unsolved problem of the hydroamination reaction is the use of aliphatic terminal alkenes without any activating groups or chelating groups as substrates,” said Professor Zhan Lu (Zhejiang University, Hangzhou, P. R. of China). He added: “The hydroamination of alkenes via metal-hydride-catalyzed hydrogen atom transfer (HAT) has been studied in detail for its excellent regioselectivity and functional group tolerance. However, due to formation of radical intermediates and the lack of suitable chiral ligands, a successful asymmetric transformation has not been reported yet.”

In a recent paper, which represents a breakthrough in the field, Professor Lu’s group developed a ligand-promoted cobalt-catalyzed Markovnikov hydroamination of alkenes via HAT process (Scheme 1a). “A wide variety of alkenes could be transformed into the corresponding amine derivatives under this mild protocol, with superb Markovnikov-type selectivity and great functional group tolerance. The newly designed un-symmetric NNN-tridentate (UNT) ligands play a key role in this transformation. Importantly, the asymmetric intermolecular hydroamination of unactivated terminal alkenes has also been achieved using chiral UNT ligands, affording good enantioselectivity,” remarked Professor Lu, who continued: “This protocol shows significant functional group tolerance under mild conditions, which offers an opportunity for late-stage hydroamination of structurally complex molecules. Besides, the products could be used to construct nitrogen-containing heterocycles and drugs, which demonstrates the usefulness of this protocol in medicinal chemistry (Scheme 1b). Additionally, simple  $\alpha$ -olefins produced in petroleum cracking, such as but-1-ene, could be converted into chiral products with good



**Scheme 1** Ligand-promoted selective hydroamination of alkenes via HAT process

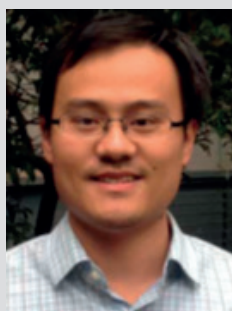
enantioselectivity (Scheme 1c). After simple recrystallization, chiral amine derivatives could be easily obtained with excellent enantiomer excess.”

Professor Lu concluded: “This study not only establishes a pathway to solve the long-standing problem in enantioselective

hydroamination of aliphatic alkenes but also suggests a potentially general strategy for asymmetric transformation of substrates without any activating or chelating groups by using earth-abundant transition metal catalysis.”

*Matthew Farah*

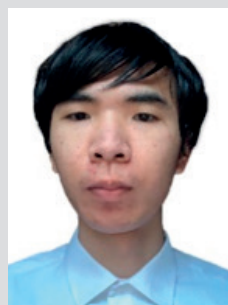
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