

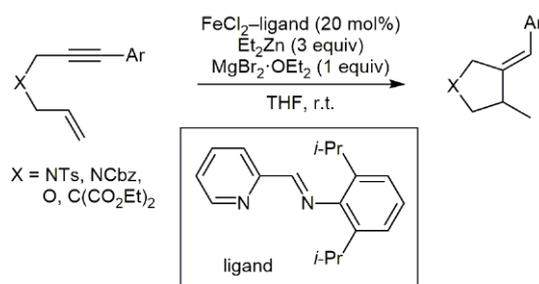
## Iron-Catalyzed Intermolecular Hydroamination of Styrenes

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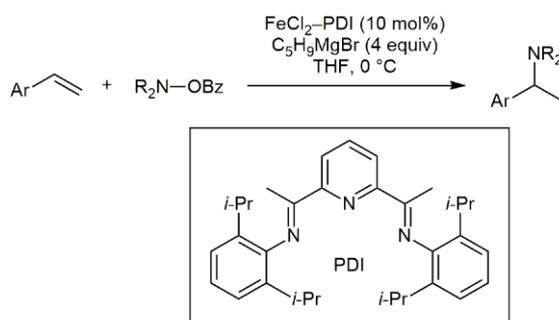
■ Functionalized benzylamines are important compounds with a number of uses as agrochemicals, intermediates in medicinal chemistry and building blocks in materials science, to cite only a few examples. Therefore, the development of novel methods for accessing this class of compounds in an efficient and economically sustainable manner continues to be an area of great interest in organic chemistry. The group of Professor Jiong Yang at Texas A&M University (USA) has an interest in low-valent iron catalysis that can be traced back to one of their natural product total synthesis projects (see: *Org. Lett.* **2010**, *12*, 5072; *J. Am. Chem. Soc.* **2012**, *134*, 8806). That work made use of a combination of  $\text{FeCl}_2$ – $\text{MeMgCl}$  and  $\text{TMSCl}$  to convert the  $\alpha,\beta$ -unsaturated ketone of carvone into an extended trimethylsilyl dienol ether. Professor Yang said: “Our curiosity about the mechanism of this unusual transformation led us to consider other possibilities of low-valent iron catalysis. Iron played an important role in the early develop-

ment of organometallic chemistry, but it has been overshadowed by late transition metals such as Pd, Rh, Ru, etc. in recent decades.” According to Professor Yang, despite the recent surge of research activities, such as the chemistry of iron-redox active ligand complexes, iron-catalyzed C–H activation, etc., the chemistry of low-valent iron remains underexplored. “We envisioned that the unique electronic structure of iron and other early transition metals could probably be translated into distinct reactivity that may be explored in transformations that have been difficult with late transition metals,” explained Professor Yang, whose group’s recent efforts have been focused on low-valent iron-catalyzed functionalization of alkenes. In collaboration with postdoctoral research associate Dr. Aijun Lin and postdoctoral fellow Dr. Zhi-Wei Zhang, they recently developed the first iron-catalyzed reductive cyclization of 1,6-enynes (*Org. Lett.* **2014**, *16*, 386).

### (A) Yang's previous work: Iron-catalyzed reductive cyclization of 1,6-enynes



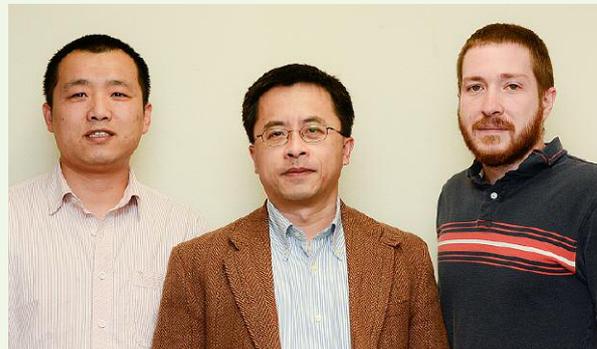
### (B) This work: Iron-catalyzed intermolecular hydroamination of styrenes



Professor Yang said: “This research project quite naturally led us to become interested in the possibility of low-valent iron-catalyzed hydroamination of alkenes using electrophilic nitrogen sources. Aijun carried out preliminary studies to verify the feasibility of the reaction before the project was transferred to the then graduate student, Bryan Huehls.” One major difficulty at that time, recalled Professor Yang, had been the low conversion of the reaction. Dr. Huehls solved this problem by literally following his nose: a distinct smell of piperidine during reaction work-up suggested that most of the electrophilic nitrogen source (*O*-benzoyl-*N*-hydroxypiperidine) had been consumed by a non-productive reduction pathway. This situation could be effectively corrected by slow addition of the electrophilic nitrogen reagent using a syringe pump. Further optimization of the reaction conditions and testing the scope of the substrates led to this iron-catalyzed intermolecular hydroamination of styrenes. According to Professor Yang, the significance of this research lies in demonstrating the possibility of low-valent iron in catalyzing transformations that have typically been reserved for late transition metals. “We are confident that further development of iron catalysis, such as by inventing new ancillary ligands, developing effective protocols to generate reactive catalytic species, and exploring new reactivities of organoiron complexes, etc. will lead to catalytic systems that are more effective and enable unique transformations that have been difficult or impossible using other transition-metal catalytic systems,” Professor Yang concluded. ■

Matteo Zanda

### About the authors



From left to right: Dr. A. Lin, Prof. J. Yang, C. B. Huehls

**Aijun Lin** was born in Jintan (P. R. of China). He received his Ph.D. from Nanjing University (P. R. of China) in 2011 for his work on asymmetric organocatalysis under the guidance of Professor Chengjian Zhu. After a one-year postdoctoral stint at the same group, he joined the research group of Professor Jiong Yang at Texas A&M University (USA) in 2012 as a postdoctoral research associate.

**C. Bryan Huehls** attended Ball State University, Indiana (USA) where he first began research in synthetic methodology under the guidance of Professor Robert E. Sammelson. After receiving his B.A. in chemistry in 2009, he started his graduate studies at Texas A&M University in spring 2010 and joined the research group of Professor Jiong Yang. His doctoral research focused on developing new methods for synthesis of indolenines and exploring iron-catalyzed transformations.

**Jiong Yang** received his Ph.D. from The Ohio State University (USA) for his work on total synthesis of natural products under the tutelage of Professor Leo A. Paquette. He pursued postdoctoral research in chemical genetics in the laboratories of Professor Peter G. Schultz (The Scripps Research Institute, La Jolla, USA) and then Professor Stuart L. Schreiber (Harvard University/Broad Institute of MIT and Harvard, USA) as an NIH postdoctoral fellow before joining Texas A&M University.