

University of Louisville
Department of Chemistry
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Literature Seminar
When: February 23, 2023
Time: **12:00 p.m.**
Location: CBL-16

Sustainable C-H Functionalization Catalyzed by Iron

Abstract:

Despite significant advancements, cross-couplings still require two pre-functionalized substrates, i.e., electrophile and nucleophile, which leads to lengthy synthetic procedures, low atom-economy, and production of stoichiometric byproducts.^[1] However, the direct transformations at C-H bonds, catalyzed by transition metals, can improve atom- and step-economy by omitting the pre-functionalization steps, leading to lower waste generation.^[1] Due to these advantages over traditional cross-couplings, C-H activation or functionalization field has grown tremendously over the past decades.^[2] Most C-H functionalization strategies rely on expensive and hazardous noble transition metals, including palladium, rhodium, and ruthenium.^[3] Recently, the necessity to switch to more environmentally friendly and sustainable platforms has prompted using earth-abundant, affordable, and often less harmful alternatives.^[3] In 1970, Kochi reported the first C-C cross-coupling pathway involving iron as an efficient catalyst.^[4] Additionally, advantages, such as, low toxicity, natural abundance, and high reactivity compared to late d -block metals, have made iron the first choice for sustainable catalysis.

Due to the importance of C-H functionalization, this presentation will focus on recent advances in iron-catalyzed C-H functionalization. We will discuss a strategy developed by Falck and coworkers for direct *meta*-selective C-H amination of benzylic and aromatic picolinates using a Fe (III) catalyst.^[5] The traditional routes for direct functionalization of electron-rich or electron-neutral substrates are challenging and require harsh reaction conditions with low regio-selectivity. However, arene *meta*-directed amination was achieved by implementing picolinate as directing group, using cost-efficient iron as a catalyst, with broad substrate scope and mild reaction conditions. Detailed mechanistic studies revealed the Fe-nitrenoid intermediate as an active catalyst. Chattopadhyay developed a unique strategy for directing group-free, selective benzylic C-H amination of challenging C(sp³)-H bond using the Iron-porphyrin complex.^[6] This work highlighted using 1,2,3,4-triazole as nitrene precursor for installing a 2-aminopyridine group to benzylic positions via the intermediacy of benzylic radical. Next, Xu and coworkers reported direct alkylation and hydroxylation of indolin-2-ones and alkyl-substituted *N*-heteroarenes through an oxidative cross-coupling.^[7] The reaction was catalyzed by inexpensive iron salt under mild ligand-free conditions using oxygen as a sole oxidant. Accordingly, all these studies highlighted the unprecedented reactivity of iron as a catalyst.

References: [1] T. Rogge, N. Kaplaneris, N. Chatani, J. Kim, S. Chang, B. Punji, L. L. Schafer, D. G. Musaev, J. Wencel-Delord, C. A. Roberts, R. Sarpong, Z. E. Wilson, M. A. Brimble, M. J. Johansson, L. Ackermann, *Nat. Rev. Methods Primers* **2021**, *1*, 43. [2] A. M. Messinis, J. C. A. Oliveira, A. C. Stückl, L. Ackermann, *ACS Catal.* **2022**, *12*, 4947. [3] P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz, L. Ackermann, *Chem. Rev.* **2019**, *119*, 2192. [4] J. D. Sears, P. G. N. Neate, M. L. Neidig, *J. Am. Chem. Soc.* **2018**, *140*, 11872. [5] R. R. Anugu, S. Munnuri, J. R. Falck, *J. Am. Chem. Soc.* **2020**, *142*, 5266. [6] H. Khatua, S. Das, S. Patra, S. K. Das, S. Roy, B. Chattopadhyay, *J. Am. Chem. Soc.* **2022**, *144*, 21858. [7] R.-M. Hu, D.-Y. Han, N. Li, J. Huang, Y. Feng, D.-Z. Xu, *Angew. Chem. Int. Ed.* **2020**, *59*, 3876.