Iron Catalyzed C–H Bond Amination: The Road to Simple, Robust and Sustainable C–N Bond Formation

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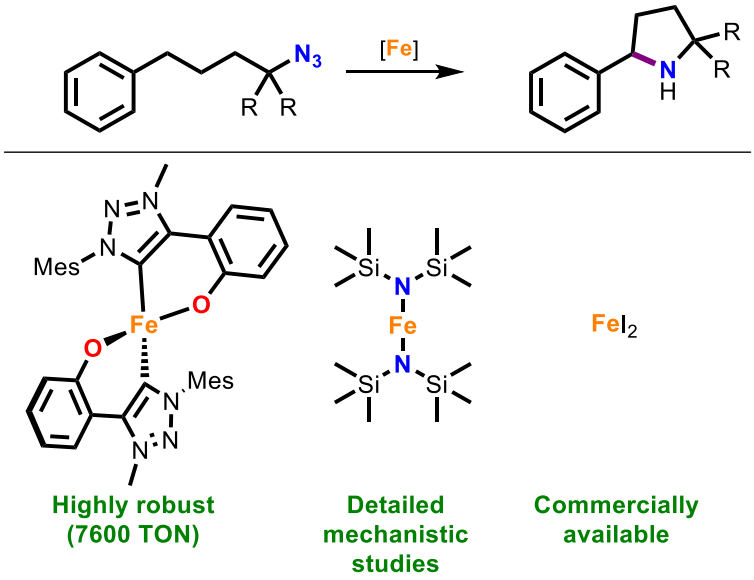
The formation of N-heterocycles is of paramount importance for synthesis of pharmaceuticals, agrochemicals and natural products. Due to its atom-economy direct C–H amination is a very attractive method to synthesize these class of compounds comparable to more traditional methods to form C–N bonds. Especially when using azides as nitrene precursors, as N_2 is produced as the only side product. Several catalysts are known to show activity in this transformation,[1] though turnover numbers were always low (single digit to a few hundreds) and required the use of stoichiometric amounts of Boc_2O to prevent product inhibitions. On top of that, the mechanism of the transformation was poorly studied.

In this contribution we describe three different iron–based catalysts that do not require the use of any additive, significantly increasing the sustainability of this transformation. One catalysts features mesoionic carbene ligands and is highly robust reaching TONs of 7600, which is an order of magnitude higher than any other reported catalyst for this reaction.[2] The second catalyst we will describe is the easily synthesized $Fe(HMDS)_2$, which reveals the detailed mechanism of the C–H amination and gives insights on how to improve the system.[3,4] The last catalyst that will be discussed is the commercially available FeI_2, making the use of this method for C–N bond formation more accessible and applicable.[5]



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[2] W. Stroek, M. Keilwerth, D. M. Pividori, K. Meyer and M. Albrecht, *J. Am. Chem. Soc.*, **2021**, *143*, 20157–20165.
[3] W. Stroek and M. Albrecht, *ChemRXiv*, **2022**, DOI: 10.26434/chemrxiv-2022-9pl01.
[4] W. Stroek, L. A. Malaspina, S. Grabowsky and M. Albrecht, **2022** *in review*
[5] W. Stroek, L. Hoareau and M. Albrecht, **2022** *in review*