

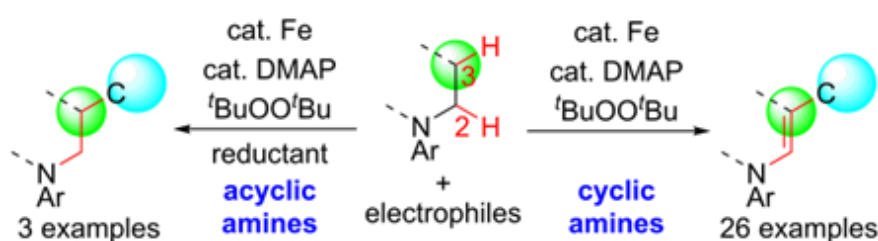
Fe-Catalyzed Oxidative C(3)-Functionalization of Amines

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Many C(3)-functionalized amines have remarkable biological activities but access to such molecules generally requires multistep, indirect pathways. Direct C(3)-functionalization of amines through catalytic conversion of an sp^3 C(3)-H bond is scarcely developed, other than the recently reported catalyses.¹ We and others previously reported oxidative C(2)-functionalizations of amines through the oxidation of amines to electrophilic imines or iminium ions, followed by addition of nucleophiles to the thus-generated electrophiles.^{2,3} In this general reaction profile, the oxidatively generated iminium ions possessing a β -hydrogen atom will isomerize to enamines in the absence of nucleophiles. The thus-generated enamines act as nucleophiles for C(3)-functionalization in the presence of appropriate electrophiles.

We will present a novel Fe-catalyzed C(3)-H functionalization of tertiary amines through such a reaction pathway.⁴ Using a catalytic amount of $FeCl_3$ and DMAP in the presence of di-*tert*-butylperoxide (TBP) as a terminal oxidant (Figure), the reaction proceeds under mild conditions to produce C(3)-functionalized amines in moderate to high yields. The reaction conditions are applicable to both cyclic and acyclic substrates under mild conditions using nitroalkenes as a coupling partner. Detailed substrate scope and mechanistic insight will be also discussed.



1. (a) Sundararaju, B.; Achard, M.; Sharma, G. V. M.; Bruneau, C. *J. Am. Chem. Soc.* **2011**, *133*, 10340. (b) Yuan, K.; Jiang, F.; Sahli, Z.; Achard, M.; Roisnel, T.; Bruneau, C. *Angew. Chem. Int. Ed.* **2012**, *51*, 8876. (c) Xia, X.-F.; Shu, X.-Z.; Ji, K.-G.; Yang, Y.-F.; Shaikat, A.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2010**, *75*, 2893.
2. Recent selected reviews: (a) Murahashi, S.; Zhang, D. *Chem. Soc. Rev.* **2008**, *37*, 1490. (b) Jones, K. M.; Klussmann, M. *Synlett* **2012**, 159.
3. (a) Hashizume, S.; Oisaki, K.; Kanai, M. *Org. Lett.* **2011**, *13*, 4288. (b) Hashizume, S.; Oisaki, K.; Kanai, M. *Chem. Asian J.* **2012**, *7*, 2600.
4. Takasu, N.; Oisaki, K.; Kanai, M. *Org. Lett.* **2013**, doi: 10.1021/ol400568u