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

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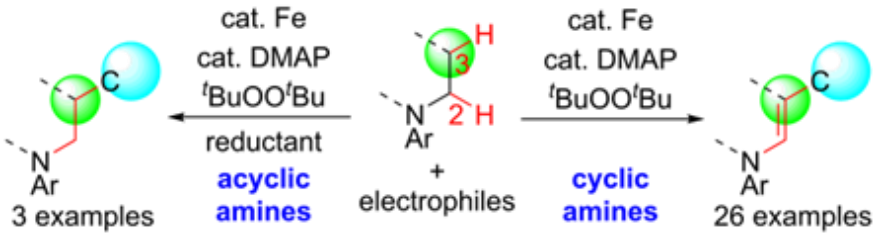
Many C(3)-functionalized amines have remarkable biological activities but access to such molecules generally requires multistep, indirect pathways. Direct C(3)-functionalization of amines through catalytic conversion of an sp^3 C(3)-H bond is scarcely developed, other than the recently reported catalyses.[1] 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.



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