Iridium(III)-catalyzed intermolecular C(sp^3)–H amidation for the synthesis of chiral 1,2-diamines

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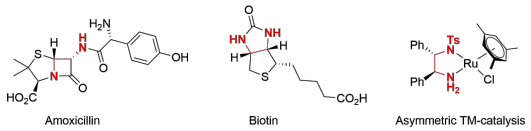
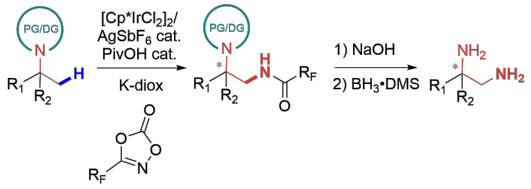
Chiral 1,2-diamines are privileged scaffolds among bioactive natural products, active pharmaceutical ingredients, ligands for transition-metal-based asymmetric catalysis and organocatalysts (Scheme 1)[1]. Although few traditional approaches have facilitated their synthesis[2], the construction of chiral 1,2-diamine motifs remains still a challenge. Lately, transition-metal-catalyzed C(sp^3)–H amination reactions have witnessed impressive advances, providing powerful, straightforward and unconventional strategies to forge new C(sp^3)–N bonds[3].



Motivated by the lack of direct methods to access such a useful scaffold, we developed an iridium(III)-catalyzed intermolecular C(sp^3)–H amidation for the synthesis of chiral 1,2-diamines (Scheme 2). This method takes advantage of the high reactivity of K-Diox[4], a bench-stable 1,4,2-dioxazol-5-one-based nitrene precursor and relies upon the design of a new, cheap and cleavable *exo*-protecting/directing group derived from camphorsulfonic acid, furnishing free enantiopure diamines upon cleavage of both nitrogen substituents[5]. Kinetic and computational studies served as support tools to gain further insights into the reaction mechanism, which proceeds through a sequence of C(sp^3)–H activation (CMD) and inner-sphere nitrene transfer. Moreover, in order to achieve the synthesis of chiral α-tertiary-1,2-diamines, a two-steps protocol involving intermolecular regioselective hydroamination of an unactivated olefin/C(sp^3)–H amidation was developed.



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