Sustainable Access to 1,3-Diamine Precursors via Iron-Catalyzed C(sp³)–H Amination of Sulfamate Derivatives

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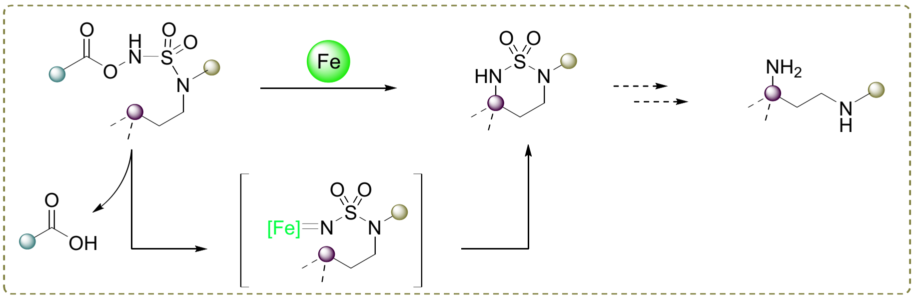
Nitrogen-based scaffolds are ubiquitous in pharmaceuticals, forming the backbone of a wide range of bioactive molecules. Among these, diamines represent an important subcategory. While the synthesis of 1,2-diamines is well established, their isomeric counterparts—1,3-diamines—remain relatively underexplored, offering both a synthetic challenge and an opportunity for innovation. Current methods for 1,3-diamine synthesis often rely on metal catalysis under harsh conditions, frequently requiring external oxidants or environmentally harmful heavy metals such as rhodium or iridium.[1] For several years, our group has been developing more sustainable processes for nitrene insertion into C=C and C(sp³)–H bonds via iron-catalyzed activation of hydroxylamine, providing a versatile route to C–N bond formation.[2] Hydroxylamine has gained recently considerable as a clean, readily available nitrene precursor. Its intrinsic oxidizing properties eliminate the need for external oxidants, offering a more sustainable and environmentally benign alternative.



In this context, the group of Eric Meggers demonstrated the efficiency of benzoylated urea-based substrates in iron-catalyzed C(sp³)–H amination, yielding five-membered imidazolidinone heterocycles as precursors to 1,2-diamines.[3] Building on this concept, our strategy involves the use of acylated sulfamate substrates to enable the selective formation of analogous six-membered sulfamate products. This approach offers a green, efficient, and operationally straightforward route to access 1,3-diamine frameworks. In this communication, we will present and discuss the optimization of the reaction conditions, along with a comprehensive analysis of the reaction's scope and limitations.

References

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[3] E. Meggers, et Al. *Angew. Chem. Int. Ed.* **2021**, *60*, 6314.