IRON-NITRENE MEDIATED INTERMOLECULAR ECO-FRIENDLY AMINATION REACTIONS

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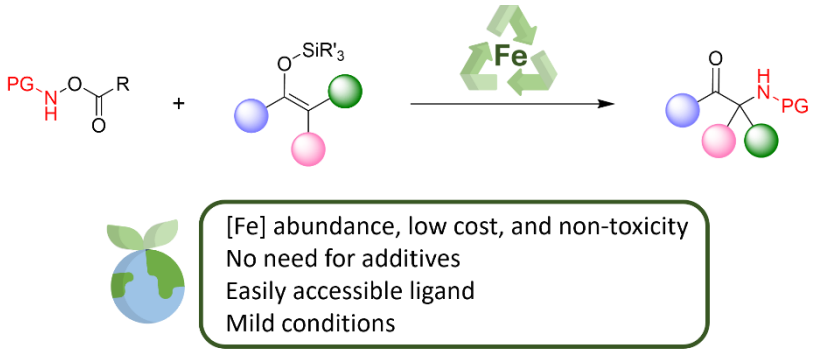
Due to the prevalence of α-amino acid and ketone moieties in natural compounds and medications the α-amination of simple ketones and esters is a crucial process in organic synthesis. Recent and straightforward approaches in this field include the development of catalytic, enantioselective α-aminations and α-oxygenations of carbonyl compounds, which are particularly useful in constructing complex natural products and bioactive molecules.[1]

Among the various amination methods, research on metallo-nitrene mediated nitrogen transfer reactions has become very popular with their ability to transfer nitrogen atoms to organic compounds. Especially iron-nitrene catalysis offers several advantages, including its abundance, low cost, and relative non-toxicity.[2] These properties make it a sustainable and attractive option for various reactions. Additionally, iron availability and environmental friendliness make it a practical alternative to other transition metals in catalysis.[3] Che highlighted the efficiency of iron complexes in intramolecular C-H amination.[4] White further underscores the diastereoselectivity of this method.[5] More recently, Strom expanded the scope to α-amination of ketones in the presence of stoichiometric oxidant showing its potential in drug discovery and natural product synthesis.[6]

Despite those developments, there are still challenges in terms of sustainable chemistry. Many studies have used potentially explosive azides as nitrogen sources or stoichiometric strong oxidants. In addition, the use of complex ligands raises questions regarding their availability. Toxic solvents and harsh reaction conditions can also be considered far from environmentally friendly chemistry.

In this communication, we will report our results towards a sustainable α-amination of silyl enol ether via iron catalysis. Optimisation of the reaction conditions, scope, and limitations of the process as well as mechanistic insights will be presented.



References

[1] J. M. Janey, *Angew. Chem. Int. Ed*. **2005**, *44*, 4292-4300.
[2] I. Bauer, H. Knölker, *Chem. Rev*. **2015**, *115*, 3170-3387.
[3] A. Correa, O. G. Mancheño, C. Bolm, *Chem. Soc. Rev*. **2008**, *37*, 1108-1117.
[4] W. Liu, D. Zhong, C. Yu, Y. Zhang, D. Wu, Y. Feng, H. Cong, X. Lu, W. Liu, *Org. Lett*. **2019**, *21*, 2673-2678.
[5] S. M. Paradine, M. C. White, *J. Am. Chem. Soc*. **2012**, *134*, 2036-2039.
[6] F. Song, S. H. Park, C. Wu, A. E. Strom, *J. Org. Chem*. **2023**, *88*, 3353-3358.