Iron-catalyzed synthesis of alpha-azido amino acids: an easy access to versatile building blocks

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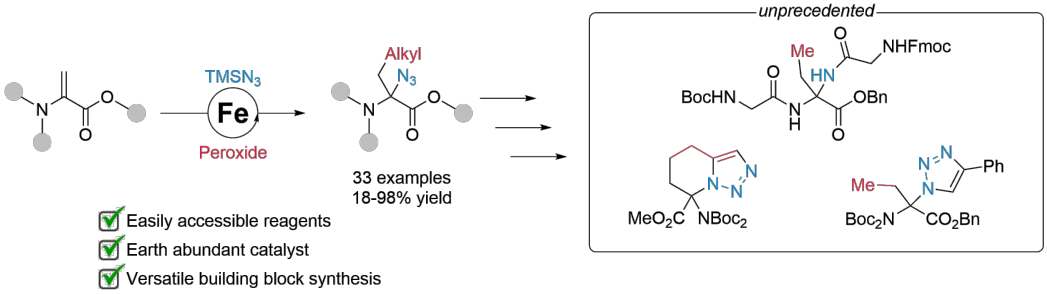
The pharmaceutical industry is interested in the development of new transformations to access diversified amino acids and peptides.[1] Non-proteinogenic amino acids (NPAAs) show great potential for the optimization of various biological properties (half-life, specificity, potency, membrane permeability and conformation) of peptide drugs.[2] However, the use of *α*-nitrogen substituted amino acids has been scarce due to their challenging synthesis.[3,4] To access these underdeveloped scaffolds, we turned ourselves to earth abundant metal catalysis. In the last decades, the use of first-row transition metals such as iron has emerged as an alternative to the well-established transition-metal catalysts such as rhodium, palladium or iridium. In addition to their high availability and reduced cost, they now appear as key catalysts for the development of new radical-mediated synthetic routes.[5] In this context, we developed an easy access to *α*-azido amino acids from dehydroamino acids as alkyl radical acceptors using iron catalysis. Various azidated amino acids, both proteinogenic and non-natural analogues, were successfully synthesized. The obtained compounds appear as versatile building blocks that could be transformed into various unprecedented scaffolds including aminal-type peptides, [7,7]-substituted tetrahydro-triazolopyridine and *α*-alkyl-α-triazole α-amino acids.[6]



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