Iridium-Catalyzed Hydrogenation of Pyridines

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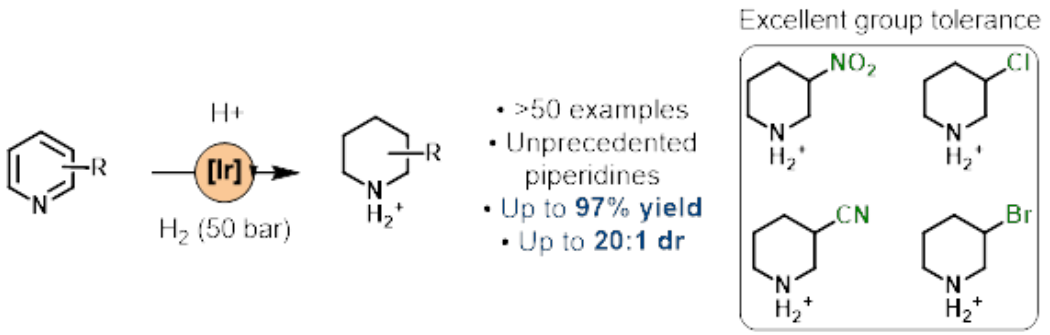
The piperidine core is present in many alkaloids and biologically relevant molecules, shows excellent pharmacological properties and is, as such, the most occurring nitrogen-heterocycle in FDA-approved drugs molecules.(1)

Out of the many ways of building complex piperidines: ring construction, ring expansion of pyrrolidines, or modification of existing piperidines(2), hydrogenation or pyridines is an attractive alternative. It takes advantage of a substantial and cheap pyridine feedstock and hydrogen gas as a priceless and harmless reducing agent offering excellent atom economy. Nevertheless, this approach to access piperidines is underdeveloped. Most pyridine reductions so far suffer from harsh reaction conditions, poor functional group tolerance, limited reaction scope, or the need to pre-functionalize the pyridine to break its aromaticity.(3)

Herein, we report a homogeneous Ir-catalyst capable of performing the mild hydrogenation of a wide range of mono- and multi-substituted pyridines. The reaction proceeds with low catalyst loading using an acid co-catalyst to break the aromaticity of the pyridine. Our method gives access to a wide variety of piperidines in excellent yields and good to excellent diastereoselectivities. Virtually any substitution pattern can be accessed with an unprecedently broad functional group tolerance that provides unique substrates, further proving the relevance of this strategy to access the undeniably valuable piperidine core.



References:

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