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Unprotected β-Arylethylamines via Iron(II)-Catalyzed 1,2-Aminoarylation of Alkenes in HFIP[1]

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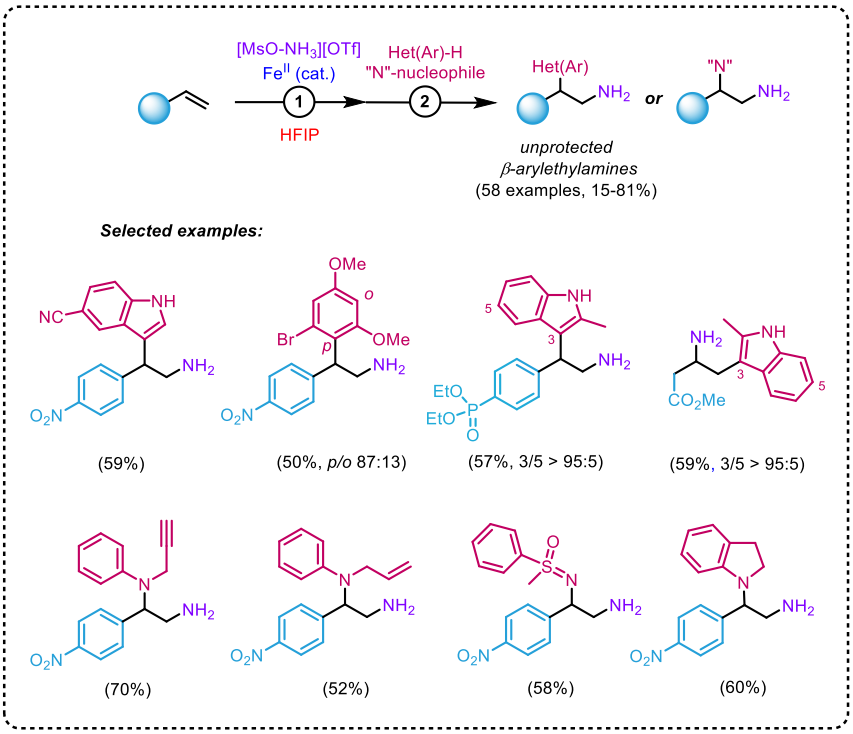

Abstract: As β-Arylethylamines are prevalent structural motifs in molecules exhibiting biological activity, we report here a sequential one-pot protocol for 1,2-aminoarylation of alkenes with hydroxylammonium triflate salts and (hetero)arenes. Hydroxylammonium triflate salts have recently gained a lot of attention as powerful reagents for the synthesis of unprotected primary amines.[2,3] Our group has a long lasting interest in the development of catalytic methodologies using HFIP as a solvent.[4] When compared to existing methods, this reaction provides a direct entry to unprotected β-arylethylamines with a remarkable functional group tolerance, allowing to install key drug-oriented functional groups in a two-step process. The methodology was recently expanded to enable alkene diamination with a wide array of N-nucleophiles bearing functional groups which were previously incompatible with superacidic medium and HFIP. The use of hexafluoroisopropanol as a solvent in combination with an iron(II) catalyst proved fundamental to facilitate these transformations towards high-value nitrogen-containing molecules. Quantification of H-bonding donor ability of HFIP by means of electrochemistry revealed its superiority over TFE or water as H-bonding activating agent, which may explain its exceptional efficiency in reactions with challenging electronically deactivated substrates.

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[3] L. Legnani, B. Morandi, *Angew. Chem. Int. Ed.* **2016**, *55*, 2248-2251
[4] V. Pozhydaiev, M. Power, V. Gandon, J. Moran, D. Lebœuf, *Chem. Commun.* **2020**, *56*, 11548-11564