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FeCl3•6H2O as efficient catalyst for one-pot synthesis of highly functionalized piperidines

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Background and Aims: Multicomponent reactions (MCRs) are a special type of synthetically useful organic reactions. MCRs are also powerful tools in medicinal chemistry and allow fast, automated, and highthroughput generation of organic compounds. The piperidine ring system is one of the most common motifs found in numerous drugs, drug candidates and natural products such as alkaloides. compounds with this ring exhibit anti-hypertensive, antibacterial, anticonvulstant, anti-inflammatory and also antimalarial activities. Also substituted piperidines have been identified as an important class of therapeutic agents in the treatment of influenza infection, cancer metastatis, viral infections including AIDS, and diabetes. Consequently, the development of efficient methods for the synthesis of this class of compounds due to their medicinal properties is a subject of considerable practical importance.
Methods: A solution of aromatic amine (2 mmol) and β-ketoester (1 mmol) in EtOH (5 mL) was stirred for 20 min in the presence of 30 mol% FeCl3.6H2O at room temperature. Next, the aromatic aldehyde (2 mmol) was added and the reaction mixture was allowed to stir for appropriate time. After completion of the reaction, the thick precipitate was filtered off and washed with ethanol (3 × 2 mL) to give the pure product.
Results: we have developed a simple and efficient method for the synthesis of highly substituted piperidines by one-pot MCR under mild conditions using FeCl3.6H2O as the catalyst in ethanol. Benzaldehydes with electronwithdrawing as well as electron-releasing groups reacted efficiently with anilines to give the corresponding piperidines in good to high yields.
Conclusions: This reaction can be regarded as an efficient approach for the preparation of synthetically and pharmaceutically important piperidine systems. This one-pot reaction has some important advantages such as the easy work-up procedure, simple and readily available precursors, high atom efficiency, clean reaction profiles, inexpensive catalyst and good to high yields.

Keywords: Multicomponent reaction; Antibacterial; FeCl3.6H2O; Piperidines; Heterocycle