



An Environmentally Friendly Procedure for the Reductive Alkylation of Amines with Ammonium Formate Using Supported Reagent

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ABSTRACT

Reductive alkylation of amines with carbonyl compounds is a useful method for the production of N-alkylated amines, a rapid, mild, efficient, inexpensive and environmentally friendly procedure is reported for the reductive alkylation of amines with aromatic aldehydes using ammonium formate and $\text{NiCl}_2/\text{SiO}_2$ with microwave heating.

KEYWORDS: reductive alkylation, ammonium formate, silica-supported reagents, N-alkylated amines

INTRODUCTION

The reaction of an aldehyde or a ketone with ammonia, primary or secondary amine in the presence of reducing agent to give N-alkylated amines is known as reductive amination of carbonyl compounds or reductive alkylation of amines. Reductive alkylation [Tarasevicha and Kozlov, 1999] of amines is a powerful and elegant methodology for the synthesis of amines and their derivatives as these compounds are highly versatile building blocks for various organic substrates and are essential precursors to a variety of biologically active compounds, such as pharmaceuticals [Merla and Risch, 2002] and agrochemicals [Sharp et al., 1988]. Amines and their derivatives have found widespread applications as solvents, raw materials for resins, textile additives, disinfectants, rubber stabilizers, corrosion inhibitors and in the manufacture of detergents and plastics.

α -Chiral amines [Nugent et al., 2006] prepared by asymmetric reductive amination of ketones frequently find use as chiral ligands, chiral auxiliaries or resolving agents. The key step in the synthesis of many alkaloid products, some agrochemicals and pharmaceutical drugs such as elanapril, lisinopril, sibutramine, rivastigmine and flomax (Figure 1) is the generation of an α -chiral amine [Blaser et al., 2002].

Reductive alkylation of amines has been found to be useful in the synthesis of benzodiazepine [Nefzi et al., 2001] derivatives, which possess an array of pharmacological activity, including antianxiety, sedative, therapeutic, anticonvulsant, muscle-relaxing and tranquilizing properties [Roma et al., 1991]. Reductive alkylation of amines has received great attention since these are important synthons for the synthesis of 2-substituted-4-amino-1,2,4,5-tetrahydro-2-benzazepine-3-ones [Rompaey et al., 2003] which showed receptor selectivity in opioid peptides [Tourwe et al., 1996], and to provide selective enzyme inhibitors [Warshawsky et al., 1996] and antigenic peptides [Casimir et al., 2000].