RUTHENIUM-CATALYZED REDUCTIVE ARYLATION OF N-(2-PYRIDINYL)AMIDES WITH ISOPROPANOL AND ARYLBORONATE ESTERS


aOrganic Synthesis, Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, B-2020 Antwerpen (Belgium)
bJanssen Research & Development, Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse (Belgium)

Amides are ubiquitous and easily accessible functional groups, making them versatile and convenient substrates for the synthesis of amines. The catalytic reduction of amides into \( \alpha \)-unbranched alkanamines has already received significant attention [1]. However, only a small number of strategies have been reported for the reductive functionalization of amides into \( \alpha \)-branched alkanamines. This reaction has a huge synthetic potential considering the carbonyl is replaced by both a carbon–carbon and a carbon–hydrogen bond. A number of pioneering reports have described such a reaction on secondary and tertiary amides. However, these reactions have some drawbacks, as they involve strongly nucleophilic and basic organometallic reactants (Li and Mg) in combination with air- and moisture-sensitive metal hydrides or silanes as reducing agents. Moreover, the amide sometimes also has to be pre-activated \textit{in situ} (e.g. Tf\(_2\)O). Amongst these reports on reductive functionalization, there are conspicuously few which describe the use of aryl nucleophiles, despite the fact that this gives rise to synthetically useful benzylamines [2]. Our group developed a novel method for the reductive arylation of amides based on a stable arylboron reactant and an alcohol, used both as reductant and solvent [3]. The method utilizes a Ru catalyst along with a Pyridine directing group (DG) on the amide nitrogen to allow reaction with the unreactive carbonyl. The DG can be easily introduced via e.g. reaction of carboxylic acid with PyNH\(_2\). The PyNH moiety in the N-Py 1-aryalkanamine product can be readily substituted with HCl giving 1-aryl-1-chloroalkane, concomitantly generating recyclable PyNH\(_2\).

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