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The Reductive Cleavage Of Picolinic Amides

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Abstract

Treatment of picolinic amides with excess zinc in aqueous hydrochloric acid at room temperature affords the corresponding amines in good to excellent yields. The mild reaction conditions exhibit useful functional group tolerance and facilitate the application of the picolinic amide moiety as a protecting group which can be easily introduced and selectively removed.

Introduction

The picolinic amide group has been used as a ligand,¹ as a protecting group,² and more recently as a directing group for transition-metal catalysed CH activation reactions.³ However, few general methods for the mild and selective conversion of picolinic amides to the corresponding amines have been reported. The most widely used procedures employ strongly hydrolytic or nucleophilic conditions at elevated temperatures,⁴ leading to poor functional group tolerance and limiting the utility of these methods in the context of complex molecule synthesis, where selectivity is desirable. Another reported cleavage reaction suggests the use of Cu (II) salts to promote the cleavage of picolinic amides,^{2b} however in our hands we found the reported conditions to afford little or no reactivity for a variety of substrates.

We therefore sought to develop a simple, high-yielding procedure to convert picolinic amides to the corresponding amines under mild reaction conditions. We were inspired by an earlier study in which Barrière and co-workers reported the reductive cleavage of the 3-hydroxy-picolinamide group within the polyamide antibiotic pristinamycin.⁵ However, in spite of detailed mechanistic investigations by the same authors,⁶ there have been no further reports

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