

Cu-CATALYZED FORMATION OF PYRIDINES FROM PROPARGYLAMINE AND CYCLOALKANONES

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Aromatic heterocycles fused with saturated cyclic hydrocarbon ring are important building blocks for medical chemistry due to their potential biological activity [1]. Such compounds can be obtained in the reactions of propargylamine and cycloalkanones catalyzed by Au(I) salts [2]. The development of noble-metal-free and reliable methods for synthesis of multi-gram amounts of the such aromatic heterocycles is important task of modern organic chemistry and catalysis. The aim of this study was to find optimal conditions for Cu-catalyzed formation of pyridines by cyclization reaction from propargylamine and cycloalkanones.

Several copper sources such as Cu(II) triflate, nitrate, chloride, pivalate and acetate were tested and anhydrous CuCl₂ was found to be the most efficient catalyst. The influence of the CuCl₂ amount in the reaction mixture on the product yield was investigated; it was found that 5 mol % was optimal content of CuCl₂. The porous coordination polymer HKUST-1 (copper(II) 1,3,5-benzenetricarboxylate) [3] was also tested as catalyst and yield of the product was 44 % after 24 h under reflux in ethanol. Notably, HKUST-1 completely dissolved in the reaction mixture thus it could not be considered as heterogeneous catalyst for the reaction. A set of solvents were tested in reflux conditions. Among ethanol, isopropanol, *tert*-butanol, isoamyl alcohol, 1,4-dioxane, hexafluoro-2-propanol the product yield was the highest in the case of isopropanol. The product yield reached the highest value after 2 h and further heating of the reaction mixture did not lead to its significant increase. Finally, ethyl-5,6,7,8-tetrahydroquinoline-6-carboxylate could be obtained in 63 % yield (Fig. 1). A series of other ketones was tested in the optimized reaction conditions.

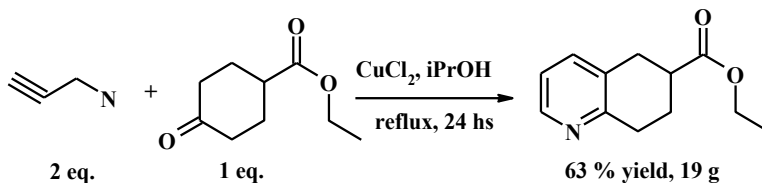


Fig. 1. The reaction of propargylamine and 4-(ethoxycarbonyl)cyclohexanone at presence of CuCl₂ as catalyst

The proposed procedure could be successfully scaled up to isolation of 19 g of ethyl-5,6,7,8-tetrahydroquinoline-6-carboxylate in one synthetic run.

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