One-step Synthesis of Functionalized Pyridines by Reaction of Propargylamine and Ketones Catalyzed by Cu(II) Compounds.

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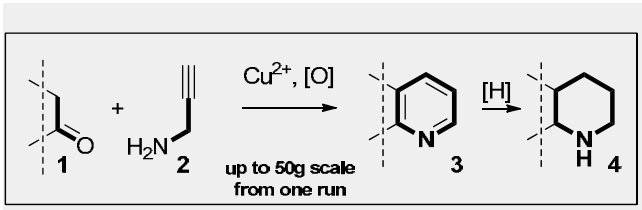
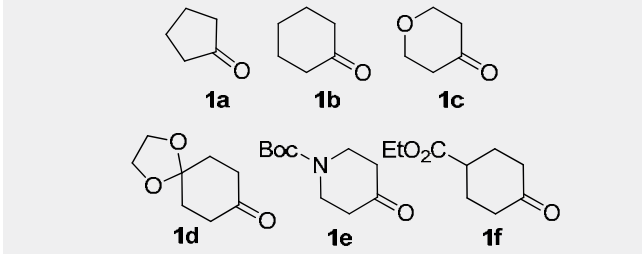
Introduction and Aim

Since the discovery of gold-catalyzed one-step amination/annulation/aromatization reaction of carbonyl compounds and propargylamine by Abbiati *et. al* in 2003 this reaction has been widely used for synthesis of functionalized pyridines. This approach allows to prepare various compounds which are hardly accessible by other synthetic routes. At present the dominating majority of reported reactions of this type were performed at presence of Au^{III} compounds or Au nanoparticles. Development of reliable method to perform this reaction at presence of 3d metals is challenging task.

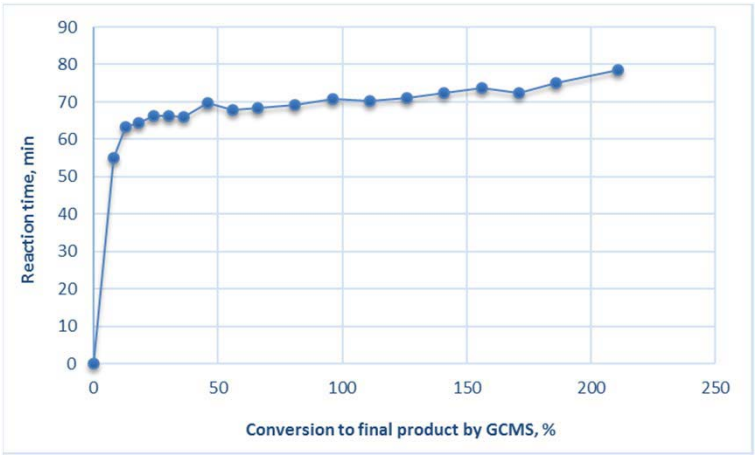
In this study we have shown that a series of cyclic ketones **1** reacted with propargylamine **2** at presence of Cu^{II} compounds ($CuCl_2$, $Cu(NO_3)_2$, $Cu_2(btc)_3$, where btc^{3-} is 1,3,5-benzenetricarboxylate) at ambient pressure upon heating with reflux.

The reaction mixtures were analyzed by HPCL and GC, while the products were identified by NMR and HPLC. It was found that $CuCl_2$ and $Cu(NO_3)_2$ as catalysts led to comparable results, while performance of $Cu_2(btc)_3$ was lower. In all cases aromatization of presumable dihydropyridine intermediate occurred due to reaction with air oxygen. The method proposed allowed to achieve 70 % yield of the pyridines **3**. Gram-scale synthesis of ethyl 6-carboxy-5,6,7,8-tetrahydroquinoline **3f** was performed using the proposed Cu-catalyzed reaction.



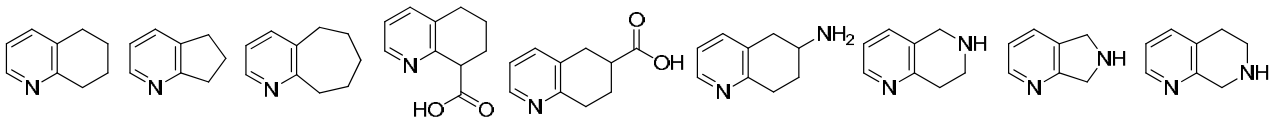


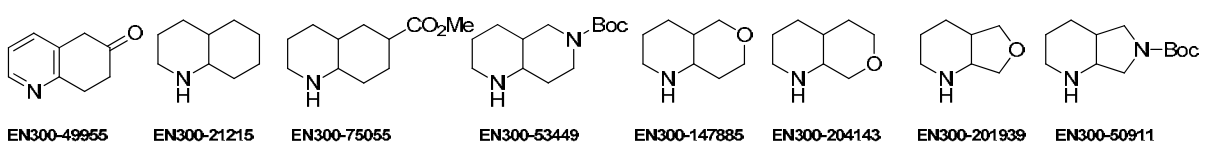
Optimization



reaction time, min	conversion by GCMS, %
0	0
8	54,98
13	63,39
18	64,37
24	66,15
30	66,15
36	66,08
46	69,6
56	67,96
66	68,42
81	69,11
96	70,88
111	70,25
126	71,07
141	72,27
156	73,79
171	72,42
186	75,17
211	78,6

Results





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