Preliminary studies on Cu/SiO_2 catalyzed imidazo[1,2-*a*]pyridine multicomponent synthesis

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INTRODUCTION

Imidazo[1,2-a]pyridines are important building blocks for development of new molecules with important biological applications. As already reported, this type of compound presents anxiolytic and sedative activities, and are commercially available as Zolpidem for example.[1] Due to this characteristics the study and development of new environment friendly methodologies are important.[2] In this context we propose the use of composite Cu/SiO_2 as an heterogeneous catalyst in the multicomponent reaction for the synthesis of this type of heterocycles.

RESULTS AND DISCUSSION

The composite Cu/SiO_2 was obtained by sol-gel process from $CuCl_2$ and TEOS with acid catalysis.[3] This composite was characterized by SEM-EDS and present superficial data of copper quantity as 0,9 $mmol.g^{-1}$. BET isotherms indicated a microporous material. This material was then applied as catalyst in the multicomponent reaction between 2-aminopyridine, benzaldehyde and phenylacetilene in 2,5 mol%.

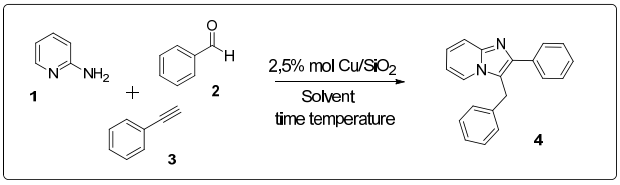
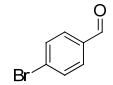
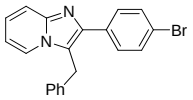
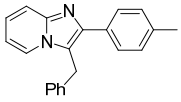
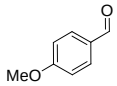
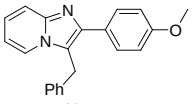
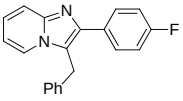
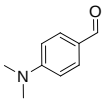
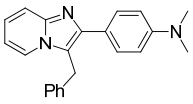
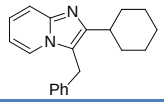


Figure 1. Imidazo[1,2-*a*]pyridines multicomponent reaction

The reaction was carried out under inert atmosphere in toluene at 120°C and the product was achieved after 48 hours in 10% yield. Increasing the catalyst load to 10 mol% and introduction of molecular sieves afforded the product in 80% yield.. A preliminary study of the reaction scope was investigated changing the aldehyde and these results are summarized in Table 1. It's worth to mention that the reaction proceeds smoothly even when electron withdrawing or donating groups are present in the aldehyde. An exception can be observed when dimethylamino benzaldehyde was used.

Table 1. Cu/SiO_2 catalyzed reaction scope

Entry	Aldehyde	Product	Yield (%)*
1			46
2			52
3			62
4			97
5			5
6			71

*Estimated by GC-MS

Several drawbacks were found in the attempts to reproduce the synthesis of the catalyst composite. We now dedicate our efforts on alternative preparation of the catalyst by modification of the sol-gel parameters to afford a robust material for further reaction investigation and catalyst recycle.

CONCLUSION

Cu/SiO_2 composite heterogeneous catalyst was found suitable for the multicomponent synthesis of substituted imidazo[1,2-*a*]pyridines. A reproducible preparation of the composite by sol-gel method is still under investigation.

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