Synthesis of tetrahydropiridines by one-pot multicomponent reaction using Niobium Pentaethoxide.

Martins, L. M.,[1]* da Silva, B. H. S. T.[1] and Silva-Filho, L. C.[1]

[1] *POSMAT - Universidade Estadual Paulista Júlio de Mesquita Filho, Bauru-SP, Brazil.*

e-mail: lmichelaomartins@yahoo.com

Keywords: Tetrahydropiridines, multicomponent reaction, niobium pentaethoxide.

INTRODUCTION

Tetrahydropiridines derivatives (THP) and theirs analogues have high pharmacological potential. That potential is explained by the piperidine subunit, present in various natural alkaloids and biologically active synthetic drugs widely used in medicine and known as a good pharmacophore (figure 1).[1] In this context, recently Misra and co-workers described excellent results obtained for antimalarial activity to THP derivatives.[2]

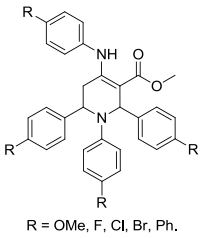
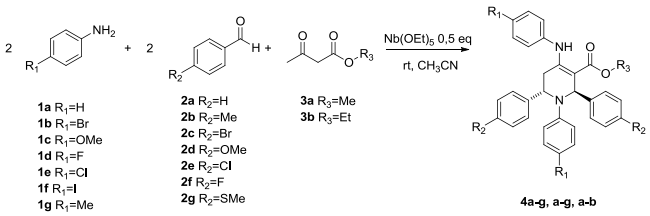


Figure 1. Tetrahydropyridine derivative

In this work, we describe our studies about the synthesis of THP derivatives by Multicomponent Reaction (MCR) catalyzed by $Nb(OEt)_5$.[3]

RESULTS AND DISCUSSION

The reactions proceeded at room temperature, in nitrogen atmosphere and anhydrous solvent (CH_3CN). We used aniline derivatives, benzaldehyde derivatives and methyl or ethyl acetoacetate, in the 2:2:1 stoichiometric ratio respectively, using 0,5 mmol of $Nb(OEt)_5$ (Scheme 1). The reactions were monitored for a time of five days, when no significant changes were observed.



Scheme 1. MCRs catalyzed by $Nb(OEt)_5$

The product obtained was purificated by recrystallization and characterized by spectroscopic and spectrometric methods. In all reactions only *trans* adduct was obtained, confirmed by NOE experiments.The reaction yields varied between 40-91% depending on the substrate. (Scheme 1 and Table 1).

Table 1. Results obtained in MCRs in the presence of $Nb(OEt)_5$.

Aniline	Aldehyde	β-ketoester	Yield (%)
1a	**2a**	**3b**	40 **(4aab)**
1b	**2a**	**3b**	48 **(4bab)**
1c	**2a**	**3b**	49 **(4cab)**
1d	**2a**	**3b**	46 **(4dab)**
1e	**2a**	**3b**	44 **(4eab)**
1f	**2a**	**3b**	53 **(4fab)**
1g	**2a**	**3b**	43 **(4gab)**
1a	**2b**	**3a**	80 **(4aba)**
1a	**2c**	**3a**	77 **(4aca)**
1a	**2d**	**3a**	81 **(4ada)**
1a	**2e**	**3a**	67 **(4aea)**
1a	**2f**	**3a**	71 **(4afa)**
1a	**2g**	**3a**	91 **(4aga)**

CONCLUSION

In conclusion, we present a efficient, and practical methodology for the preparation of tetrahydropiridines derivatives through Multicomponent reaction catalyzed by $Nb(OEt)_5$. The method offers several advantages such as Atom economy, good yields, environmentally benign, and mild reaction conditions.

ACKNOWLEDGEMENTS

The authors thanks to **FAPESP, CAPES and CNPq** for financial support.

REFERENCES

[1] Botté, C.Y.; Dubar, F.; McFadden, G. I.; Maréchal, E.; Biot, C. *Chem. Rev.* **2012**, *112*, 1369.

[2] Misra, M.; Pandey, S. K.; Pandey, V. P.; Pandey, J.; Tripathi, R.; Tripathi, R. P. *Bioorg. Med. Chem.* **2009**, *17*, 625.

[3] Lacerda Jr., V.; dos Santos, D. A.; Silva-Filho, L. C.; Greco, S. J.; dos Santos, R. B. *Aldrichimica Acta* **2012**, *45*, 19.