Synthesis of 2,3-Diaryl-2-azabicyclooctanones derivatives by multicomponent reaction promoted by $Nb(OEt)_5$.

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INTRODUCTION

The 2,3-Diaryl-2-azabicyclooctanones derivatives (**1**) can be synthetized by Povarov Multicomponent Reaction (MCR) using a Lewis Acid as reaction promoter.[1,2] The Povarov MCRs are defined as a process in which three or more reagents are combined in the same reaction "pot" generating the products with good structural complexity, with characteristics of each reagent used and in a single step.

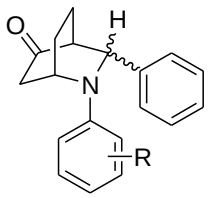

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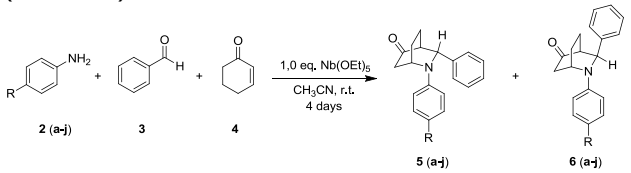
Figure 1. 2,3-Diaryl-2-azabicyclooctanones derivatives.

In studies recently found in the literature,[1,2] we can observe the good applicability of 2,3-Diaryl-2-azabicyclooctanones derivatives as possible drugs for the treatment of Alzheimers's disease. The azabicyclooctanones derivatives act by inhibiting the acetylcholinesterase (AChE), an enzyme responsible by the hydrolysis of acetylcholine in the brain.[1,2]

In this work we report a new method to synthesize 2,3-Diaryl-2-azabicyclooctanones derivatives through Povarov MCRs, using niobium pentaethoxide as a reaction promoter.[3]

RESULTS AND DISCUSSION

The MCRs were conducted between anilines derivatives {**2**(**a**-**j**)}, benzaldehyde (**3**) and ciclohexen-2-one (**4**), using niobium pentaethoxide. (scheme1)



Scheme 1: MCR using $Nb(OEt)_5$ as promoter.

The reactions were realized at room temperature and under inert atmosphere, using anhydrous CH_3CN. The products obtained were isolated by silica-gel column chromatography and characterized through spectroscopic and spectrometric methods.

The results obtained are described in the table 1.

Table 1. Results obtained at MCR promoted by $Nb(OEt)_5$.

Aniline	R	Yield (%)	Products Ratio (%)
2a	H	80	60:40 (**5a**:**6a**)
2b	F	94	49:51 (**5b**:**6b**)
2c	Cl	78	48:52 (**5c**:**6c**)
2d	Br	86	45:55 (**5d**:**6d**)
2e	I	86	46:54 (**5e**:**6e**)
2f	Me	93	61:39 (**5f**:**6f**)
2g	Et	95	59:41 (**5g**:**6g**)
2h	n-Bu	84	60:40 (**5h**:**6h**)
2i	t-Bu	94	68:32 (**5i**:**6i**)
2j	OMe	74	57:43 (**5j**:**6j**)

Analyzing the data above, we can verify that the $Nb(OEt)_5$ promotes the MCR to synthesize the 2,3-Diaryl-2-azabicyclooctanones derivatives with high yield and moderate reaction time.

CONCLUSION

The results obtained in this work show that the $Nb(OEt)_5$ is a good promoter to act as Lewis Acid in the preparation of 2,3-Diaryl-2-azabicyclooctanones derivatives, obtaining the products with high yield.

ACKNOWLEDGEMENTS

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