Novel Photoactive N-Heterocycles Bearing a Benzoxazole Moiety: Synthesis and Photophysical study

Ricardo F. Affeldt (PG)*, Dennis Russowsky (PQ), Fabiano S. Rodembusch (PQ)

Depto. de Quím.Orgânica UFRGS Av. Bento Gonçalves, 9500. Porto Alegre – RS. CEP 91501-970.

** Corresponding author: r.affeldt@gmail.com*

Keywords: 1,4-dihydropyridines, fluorescence, benzoxazole

INTRODUCTION

The 2-(2'-hydroxyphenyl)benzoxazole (HBO) has been receiving considerable attention during the past decades concerning its application as high-intense fluorescent probe.[1] On the other hand, 1,4-dihydropyridines (1,4-DHP) are small molecules recognized for their pronounced bioactivity as calcium channel blockers.[2] Structurally, the 1,4-DHPs are biommimetic analogues of the NADH coenzyme, which has also application as fluorescent probe in biological fermentations. Herein, we describe the synthesis and photophysical study of new 1,4-DHPs bearing the fluorescent HBO moiety.

RESULTS AND DISCUSSION

In order to synthesize intense fluorescent 1,4-DHPs, a method for obtaining the precursor 5-formil-2-(2'-hydroxyphenyl)benzoxazole (HBOCHO) had to be designed. The synthesis was developed in two steps consisting on condensation of 2-aminophenol and salicylic acid to afford HBO and further formylation step with hexamethylenetetramine yielding the desired product (Figure 1).

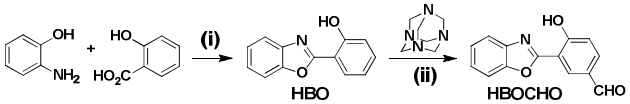

Figure 1. Synthesis of HBOCHO. Conditions: **(i)** PPA, 175°C, 5h. Yield 57% **(ii)** PPA, 100°C, 4h. Yield 30%.

The novel N-heterocycles (HBODHP) were achieved by Hantzsch multicomponent condensation catalyzed by $InCl_3/SiO_2$ composite[3] (Figure 2).

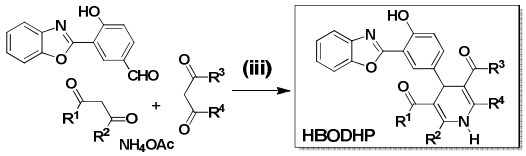

Figure 2. Multicomponent synthesis of HBO-DHPs. Conditions: **(iii)** $InCl_3/SiO_2$ (10 mol%), *i*PrOH, reflux, 3h.

Three new fluorescent heterocycles were obtained varying ethyl acetoacetate and dimedone in different combinations (Table 1). These combinations were chosen due to similarity of the desired products with known bioactive molecules. The reaction was carried out under reflux. The catalyst and the pure product were removed from the crude mixture by simple filtration.

Table 1. Multicomponent synthesis of HBODHPs.

Ent.	R^1	R^2	R^3	R^4	Yield
1	Me	OEt	Me	OEt	46%
2	$-CH_2C(CH_3)_2CH_2-$		$-CH_2C(CH_3)_2CH_2-$		50%
3	Me	OEt	$-CH_2C(CH_3)_2CH_2-$		66%

To enhance the applicability of these privileged compounds, their oxidation were performed (Figure 3) leading to a pyridine derivative (HBOPy) aiming different photophysical properties.

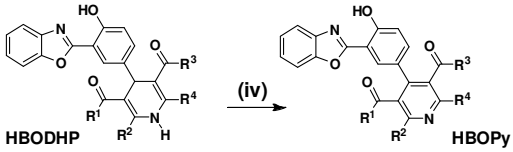

Figure 3. Oxidation of HBODHPs. Conditions: **(iv)** I_2 2eqv., MeCN, reflux, 5h. Yield 70-90%.

The HBODHP (Table 1, ent. 1) presents in acetonitrile an absorption band located at 333 nm and a fluorescence emission located at 473 nm. The oxidized HBODHP shows absorption and fluorescence emission maxima red-shifted 2 nm (335 nm) and 14 nm (487 nm) respectively, as expected, since the conjugation length was increased. All fluorescence results indicate that a phototautomerism takes place in the excited state.

CONCLUSION

Novel fluorescent 1,4-dihydropyridines were successfully synthesized by Hantzsch multicomponent reaction using a new benzoxazole dye. The 1,4-DHPs and its oxidized analogues presented absorption in the UV region and fluorescence emission in the blue-green region.

ACKNOWLEDGEMENTS

CNPq and INDI-Saúde for financial support.

REFERENCES

[1](a) Abou-Zied, O.K. *Chem. Phys.* **2007**, *337*, 1. (b) Demchenko, A.P. *et al. J. Fluor.* **2010**, *20*, 1099.
[2] Bossert, F. *et al. Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 762.
[3] Affeld, R.F.; Russowsky, D. *XXXI RASBQ*, **2008**, Águas de Lindóia/SP.