Synthesis and photophysics of new fluorescent Biginelli compounds via MCR. A potential molecular probes.

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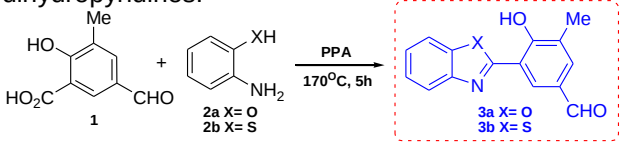
Abstract

The fluorescent aldehydes **3a-b** were synthesized and applied in the Biginelli MCR to afford new photoactive DHPMs **6a-b**. A photophysical study was performed in order to explore these compounds as potential molecular probes.

Introduction

Molecular imaging based in use of fluorescence has been applied successfully to visualization of biological processes and pathologic conditions in cells or tissues.[1] The development of highly sensitive molecular probes remains a challenge for the visualization of molecular events in cancer tumors.[2]

In order to propose a new family of potential molecular probes, the aldehydes **3a-b** were prepared similarly as previously described for the MCR synthesis of fluorescent Hantzsch 1,4-dihydropyridines.[3]

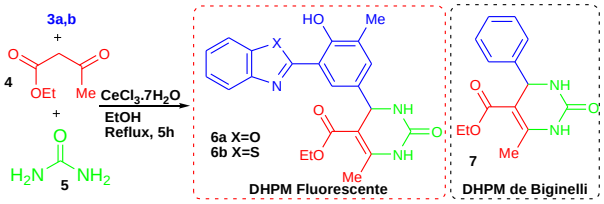


Scheme 1. Synthesis of fluorescent aldehydes **3a,b**.

The main objective is to prepare fluorescent DHPMs serving as potential molecular probes.

Results and Discussion

The 3,4-dihydropyrimidinones (DHPM) are nitrogen containing heterocycles that show a variable biological activities, including anti-proliferative activity against a series of cancer cell lines.[4]



Scheme 2. Preparation of fluorescent Biginelli DHPMs.

Their synthesis was performed via the Biginelli MCR between the aldehydes **3a-b**, ethyl acetoacetate (**4**) and urea (**5**) in presence of $CeCl_3.7H_2O$ as Lewis acid catalyst, to afford the respective DHPMs **6a-b** in 60% and 55% yield, respectively after purification by column chromatography. The DHPM **7** was prepared in the same way in 79% yield. (Scheme 2).

Compounds **6a-b** present absorption maxima ascribed to ππ* electronic transitions (ε 10^4 M^{-1}·cm^{-1}), located at 327 and 340 nm, respectively in despite of the non-ESIPT compound **7** (284 nm). Compounds containing the benzazole moiety present fluorescence emission in the blue-green regions (**6a**= 534 nm and **6b**= 500 nm) with a large Stokes' shift (**6a**= 207 nm and **6b**=160 nm, Figure 1).

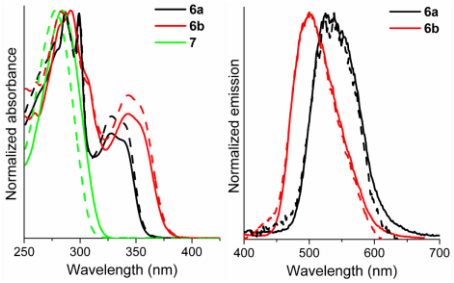


Figure 1. Normalized UV-Vis absorption and fluorescence emission of **6a,b** and **7** in ethanol (solid line) and dichloromethane (dash line).

These results indicate the feasibility of synthesize fluorescent 3,4-dihydropyrimidinones and explore their use as possible molecular probes.

Conclusion

The large Stokes' shift observed for the compounds **6a-b** indicate their potential use as Molecular Probes in investigations of cellular events in the molecular level. A series of others different fluorescent-DHPMs are under current investigation.

Acknowledgements

FAPERGS CNPq CAPES PPGQ UFRGS

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