



Multicomponent one-pot synthesis of luminescent imidazo [1,2-*a*]pyridine-3-amines. Studies of fluorescence, solvatochromism, TD-DFT calculations and bioimaging application

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ABSTRACT

Herein we report on a novel series (**4a-4p**) of fluorescent Imidazo [1,2-*a*]pyridines (IMPs) synthesized via an eco-friendly microwave-assisted Groebke-Blackburn-Bienaymé reaction (GBBR), in good to excellent yields (80–92%) and under a green catalyst. The target molecules absorb at the UV-vis region and emit from blue- to greenish fluorescence with relatively large Stokes shifts (6780–9011 cm⁻¹) due to an Intramolecular Charge Transfer (ICT) process from the strong donor triphenylamine (TPA) to the acceptor Imidazo [1,2-*a*]pyridine. Time dependent DFT calculations were performed to interpret the structure-property relationships and corroborate the ICT character and assess their energy band gaps. In addition, imaging studies of the HEK293 and HeLa cell lines revealed that the IMP **4e**, with the highest quantum yield of fluorescence (ϕ_f) of 66%, is a specific blue fluorescent probe to stain the DNA of the nucleus.

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1. Introduction

The design of novel fluorescent organic compounds is a very active research area which has provided during the last two decades guidelines for the development of probes for biomedical applications, including bio-sensing and bio-imaging. [1–3] In the design of novel fluorophores, the nature of the electron donor-acceptor groups, substituents and π -connectors are key factors which play systematic and complementary roles to tailor the photophysical and electrochemical properties, *i.e.*, tune the energy gap between the HOMO and LUMO levels, enhance luminescence, provide an efficient ICT character to the compound, improve chemical affinity to biomolecules, among others. [4]

IMPs [5–6] have been employed successfully as probes for bioimaging [7–9] and chemosensor applications. [10–11] In addition, IMPs have been reported to exhibit Excited-State Intramolecular Proton Transfer (ESIPT) and aggregation induced emission.

[12] Despite these reports effectively exemplifying the advantages offered by IMPs, their synthesis implied large number of reagents, high temperatures, long reaction times and in some cases overall yields from low to moderate. [5–12]

Efficient and versatile synthetic tools such as Multicomponent Reactions (MCRs) [13–15] for fluorescent IMPs have become prominent with several advantages including high convergency, broad scope, atomic economy, operational simplicity, eco-friendliness or mild conditions and good overall yields. However, the Isocyanide-based multicomponent reaction (IMCR) such as the Groebke-Blackburn-Bianymé reaction (GBBR) and the application of GBB fluorescent products in bioimaging has not received sufficient attention. [16–18] Lavilla et al. synthesized and assessed the cell permeability of a fluorescent BODIPY-based IMP (Scheme 1a) by imaging its localization in live A549 cells, resulting in the staining of cytoplasm and some lysosomes. [7]

On other hand, triphenylamine (TPA) is one of the most useful electron-donating scaffolds to produce different types of fluorescent probes. It is widely used in the fields of molecular recognition, bioimaging, materials chemistry and medicinal chemistry. [19] In 2014, Nagarajan et al. synthesized IMPs having TPA at the C-2 po-

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