

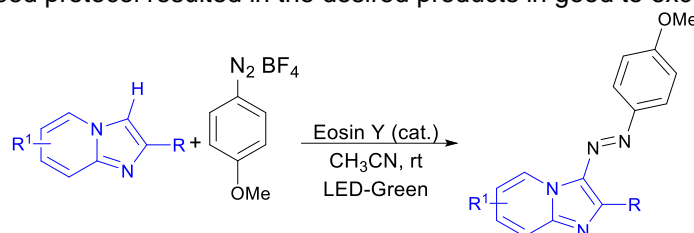
EOSIN Y-CATALYZED PHOTO-INDUCED DIRECT C(sp²)-H BOND AZO COUPLING OF IMIDAZO-HETEROARENES WITH 4-METHOXYBENZENE DIAZONIUM TETRAFLUOROBORATE

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Resumo

In this report, a highly efficient Eosin-Y-catalysed direct C(sp²)-H bond azo coupling of imidazo-heteroarenes with 4-methoxybenzene diazonium tetrafluoroborate was achieved using sustainable approaches. This acid-free, photo-induced protocol resulted in the desired products in good to excellent yields.



Graphical Abstract

Palavras-chave: Green chemistry, Photo-catalysis, organic synthesis.

Apoio financeiro: PIBIC, CNPQ, CAPES.

Trabalho selecionado para a JNIC: UFSC, UFMS.

Introdução

The imidazo[1,2-a]pyridine (**IP**) core, found in many bioactive natural products and pharmaceuticals, represents an important “privileged scaffold.”^[1] Several commercially available drugs, e.g., alpidem, necopidem and saripidem (as anxiolytics), zolpidem (as a sedative), miroprofen (as an analgesic) and zolimidine (in the treatment of peptic ulcer) (Figure 1a-d),^[1a,2] have the **IP** moiety in their core structure. Besides, aryl-azo compounds are widely used in several areas, including the chemical industry, pharmaceuticals, chemo-sensors, electronics and liquid crystals (1e-f, Figure 1).^[3]

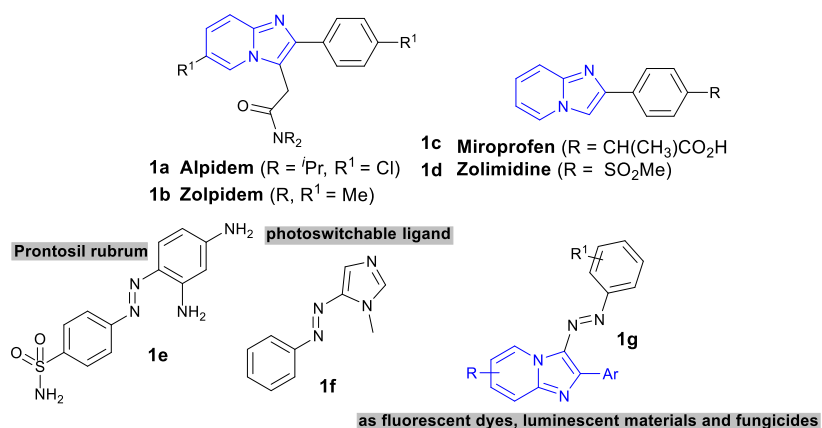


Figure 1. Examples of important azole-heterocyclic azo derivatives.

The development of new synthetic procedures to obtain multi-targeted hybrids of these skeletons (aryl-azo imidazo[1,2-a]pyridine) in a single structure would be useful, due to their diverse applications (**1g**, Figure 1).^[4]

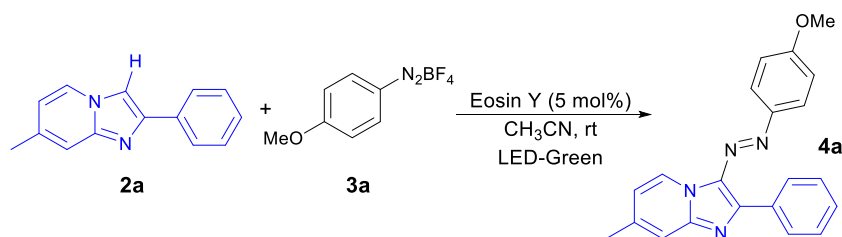
As part of our research interest in designing and developing sustainable processes as well as in the C(sp²)-H functionalization of biologically relevant heteroarenes,^[5] herein, we disclose for the first time a photo-induced eosin Y-catalyzed azo coupling of imidazo-heteroarenes with 4-methoxybenzene diazonium tetrafluoroborate.

Metodologia

Proton nuclear magnetic resonance spectra (^1H NMR) were obtained at 200 MHz on a Bruker AC-200 NMR spectrometer or at 400 MHz on a Varian AS-400 NMR spectrometer. Spectra were recorded in CDCl_3 solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of CDCl_3 or tetramethylsilane (TMS) as the external reference. High resolution mass spectra were recorded on a Bruker microTOF-Q II APPI/APCI mass spectrometer equipped with an automatic syringe pump for sample injection. The melting points were determined in a Microquímica MQRPF-301 digital model equipment with heating plate. Column chromatography was performed using Silica Gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck Silica Gel GF₂₅₄, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor and acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material.

Resultados e Discussão

For the optimization of this azo-coupling via $\text{C}(\text{sp}^2)\text{-H}$ bond functionalization, we used 7-methyl-2-phenylimidazo[1,2-*a*]pyridine **2a** and 4-methoxybenzene diazonium tetrafluoroborate **3a** as model substrates. Ideal condition was achieved by using one equiv. **2a** and one equiv. of **3a**, eosin Y (5 mol%) as a catalyst and 2 mL CH_3CN under irradiations of green LED, with a reaction time of 2 h at rt (Scheme 1).



Scheme 1. Optimized reaction condition using **2a** and **3a** as substrates

With the best reaction parameters in hand, the generality and scope of the $\text{C}(\text{sp}^2)\text{-H}$ bond azo coupling of other imidazo[1,2-*a*]pyridine (IPs) **2** with 4-methoxybenzene diazonium tetrafluoroborate **3a** were investigated (Figure 2).

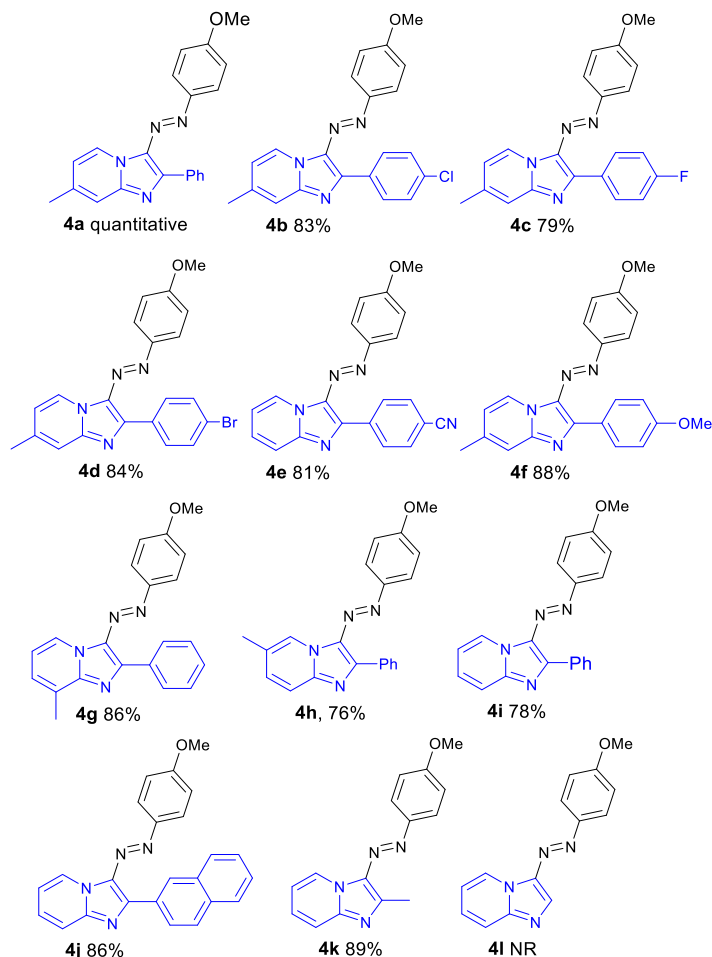


Figure 2. Scope of the reaction.

Conclusões

In conclusion, we have developed an acid free, eosin Y-catalyzed procedure for the direct C(sp²)-H bond azo coupling of imidazo[1,2-a]pyridine (IPs) **2** with 4-methoxybenzene diazonium tetrafluoroborate **3a**. Under the optimized reaction conditions, this photo-redox approach worked efficiently to form the azo products in good to excellent yields.

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