

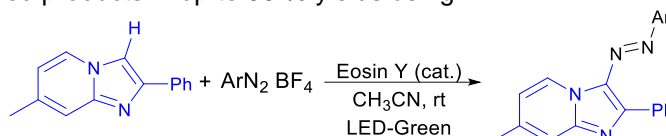
VISIBLE-LIGHT-PROMOTED, AZO COUPLING OF 7-METHYL-2-PHENYLIMIDAZO[1,2-A]PYRIDINE WITH ARYL DIAZONIUM SALTS VIA C(SP²)-H BOND FUNCTIONALIZATION

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Resumo

Highly efficient Eosin-Y-catalysed direct C(sp²)-H bond azo coupling of 7-methyl-2-phenylimidazo[1,2-a]pyridine with substituted aryl diazonium tetrafluoroborate was achieved under acid free-conditions. This approach afforded the desired products in up to 99 % yields using.



Graphical Abstract

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

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Introdução

Imidazo[1,2-a]pyridines (IP) are ubiquitous heterocycles that represent an important “privileged scaffold”.^[1,2] Their structure is present in many pharmaceuticals (**1a-f**, Figure 1) and also has applications in material sciences.^[3,4] Therefore, it is not surprising that the synthesis and functionalization of imidazo-heteroarenes have received considerable attention in different areas of scientific research.^[1,2,5,6] Analogously, aryl-azo compounds are widely used in several areas, including the chemical industry, pharmaceuticals, chemosensors, electronics and liquid crystals (**1g-j**, Figure 1).^[7,8]

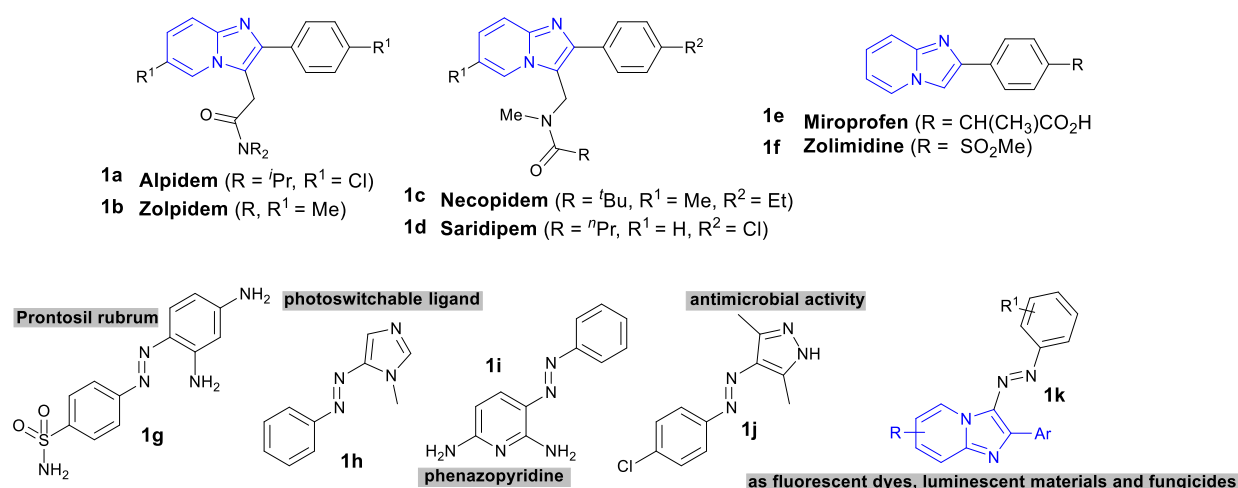


Figure 1. Examples of important azole-heterocyclic azo derivatives.

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 (**1k**, Figure 1).^[9]

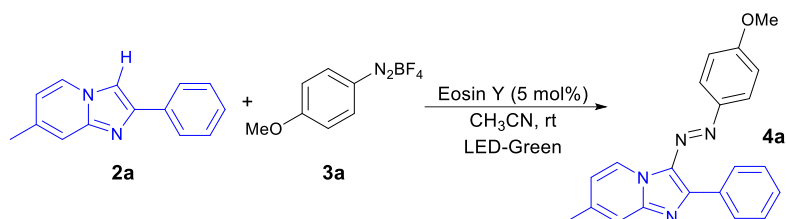
In relation to our continuing interest in the functionalization of heteroarenes as well as in the design of eco-friendly processes,^[10-15] herein we report, for the first time a photo-induced eosin Y-catalyzed azo coupling of 7-methyl-2-phenylimidazo[1,2-a]pyridine with substituted aryl diazonium tetrafluoroborate.

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 7-methyl-2-phenylimidazo[1,2-*a*]pyridine **2a** with other substituted aryl diazonium tetrafluoroborate **3** were investigated (Figure 2).

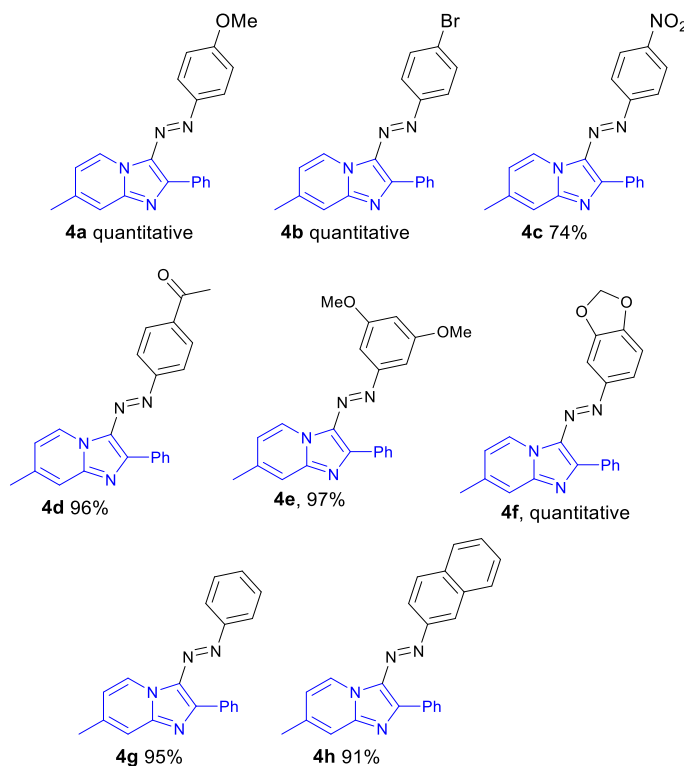


Figure 2. Scope of the reaction.

Conclusões

In conclusion, we have developed a greener, eosin Y-catalyzed procedure for the direct $\text{C}(\text{sp}^2)\text{-H}$ bond azo coupling of 7-methyl-2-phenylimidazo[1,2-*a*]pyridine **2a** with other substituted aryl diazonium tetrafluoroborate **3**. Under the optimized reaction conditions, this photo-redox approach worked efficiently to form the azo products in good to excellent yields. This is an important contribution considering the mildness of the reaction conditions as well as the potential therapeutic application of these compounds.

Referências bibliográficas

- [1] A. K. Bagdi, S. Santa, K. Monjr, A. Hajra, *Chem. Commun.*, 2015, **51**, 1555.
- [2] A. K. Bagdi, ; A. Hajra, *Chem. Rec.*, 2016, **16**, 1868.
- [3] L. A. Sorbera, J. Castañer, P. A. Leeson, *Drugs Future*, 2002, **27**, 935.
- [4] A. Douhal, F. Amat-Guerri, A. U. Acuna, *Angew. Chem. Int. Ed.*, 1997, **36**, 1514.
- [5] C. Ravi, S. Adimurthy, *Chem. Rec.*, 2017, **10**, 1019.
- [6] J. Rafique, S. Saba, M. S. Franco, L.; Bettanin, A. R. Schneider, L. T. Silva, A. L. Braga, *Chem. Eur. J.*, 2018, **24**, 4173.
- [7] B. Xiong, G. Wang, L. Wang, T. Xiong, C. Zhou, Y. Liu, P. Zhang, C. Yang, K. Tang, *ChemistrySelect*, 2018, **3**, 5147.
- [8] T. Wendler, C. Schütt, C. Näther, R. Herges, *J. Org. Chem.*, 2012, **77**, 3284.
- [9] T. Yen, X. Li, J. Kunlun, C. Weiliang, Z. L. Baoliu, Z. Wenxu, L. Chunyuan, Imidazo heterocyclic azo derivative and preparation method and application thereof, 2016, CN105713015A (Patent).
- [10] J. Rafique, S. Saba, A. R. Rosário, A. L. Braga, *Chem. Eur. J.*, 2016, **22**, 11854.
- [11] J. Rodrigues, S. Saba, A. C. Joussef, J. Rafique, Braga, A. L. *Asian J. Org. Chem.*, 2018, **7**, 1819.
- [12] Y. H. Matzkeit, B. L. Tornquist, F. Manarin, G. V. Botteselle, J. Rafique, S. Saba, A. L. Braga, J. F. Felix, R. Schneider, *J. Non-Cryst. Solids*, 2018, **498**, 153.
- [13] a) M. M. Peterle, M. R. Scheide, L. T. Silva, S. Saba, J. Rafique, A. L. Braga, *ChemistrySelect*, 2018, **3**, 13191; b) J. Rafique, S. Saba, T. E. A. Frizon, A. L. Braga, *ChemistrySelect*, 2018, **3**, 328; c) L. Bettanin, S. Saba, F. Z. Galetto, G. A. Mike, J. Rafique, A. L. Braga, *Tetrahedron Lett.*, 2017, **58**, 4713.
- [14] J. Rafique, S. Saba, A. R. Schneider, M. S. Franco, S. M. Silva, A. L. Braga, *ACS Omega*, 2017, **2**, 2280.
- [15] G. M. Almeida, J. Rafique, S. Saba, T. Siminski, N. S. R. S. Mota, D. W. Filho, A. L. Braga, R. C. Pedrosa, F. Ourique, F. *Biochem. Biophys. Res. Commun.*, 2018, **503**, 1291.