

SEPTEMBER
23-27TH
2024

19TH BMO S

BRAZILIAN MEETING
ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

Radical C3-alkylation of coumarin via Pd-photocatalyzed Heck reactions

Camila Pelizzer de Oliveira,¹ Clarice Alves Dale Caiuby,¹ Marco Antonio Barbosa Ferreira^{1*}

¹ Department of Chemistry, Federal University of São Carlos, UFSCAR, 13565-905

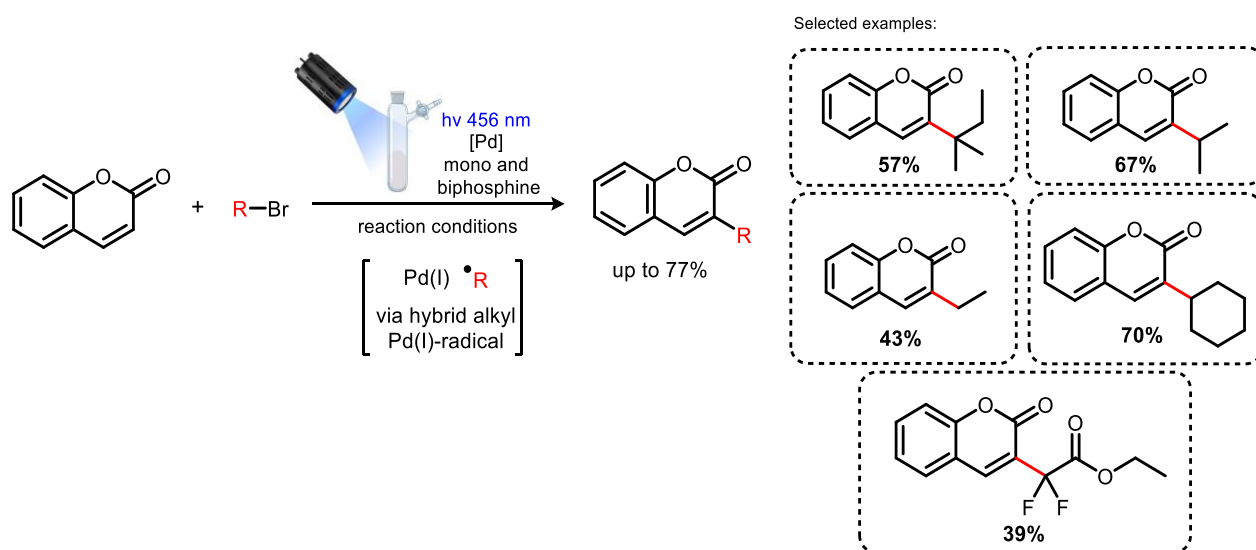
*e-mail: marco.ferreira@ufscar.br

Keywords: Transition Metal Catalysis, Photochemistry, Coumarin, Organic Synthesis.

ABSTRACT

Coumarin derivatives, known for their important bioactivities, are frequently used in medicinal chemistry.¹ Functionalization at the C3 position of coumarins represents a valuable synthetic approach to modulate their biological properties. However, metal-catalyzed general methodologies for direct installation of alkyl groups in coumarins with high regioselectivity are still limited. Traditional methods based on cross-coupling reactions use excess oxidant and high temperatures,² which can often limit the scope of the reaction.

In this work, we achieved the C3-alkylation of coumarins through a palladium-photoredox Heck reaction using alkyl halides as radical precursors; an effective strategy to the formation of C–C bonds under mild conditions using visible light as energy source.³ This transformation is catalyzed by a photoactive complex formed from a palladium source and the combination of mono- and biphosphines as ligands. Furthermore, primary, secondary, and tertiary alkyl bromides were successfully used as substrates, resulting in the formation of the desired products as a single regioisomer in up to 77% yield.



ACKNOWLEDGEMENTS



(2023/05757-4); (2020/10246-0);
(2022/11314-5); (2021/12394-0);
(2022/14197-0).



REFERENCES

References: ¹ (a) Matos, M. J.; Vazquez-Rodriguez, S.; Santana, L.; Uriarte, E.; Fuentes-Edfuf, C.; Santos, Y.; Muñoz-Crego, A. *Med. Chem.* **2012**, *8*, 1140. (b) Matos, M. J.; Vazquez-Rodriguez, S.; Santana, L.; Uriarte, E.; Fuentes-Edfuf, C.; Santos, Y.; Muñoz-Crego, A. *Molecules* **2013**, *18*, 1394. (c) Gualandi, A.; Rodeghiero, G.; Della Rocca, E.; Bertoni, F.; Marchini, M.; Perciaccante, R.; Jansen, T. P.; Ceroni, P.; Cozzi, P. G. *Chem. Commun.* **2018**, *54*, 10044. ² (a) Min, M.; Kim, Y.; Hong, S. *Chem. Commun.* **2013**, *49*, 196. (b) Jafarpour, F.; Hazrati, H.; Mohasselyazdi, N.; Khoobi, M.; Shafiee, A. *Chem. Commun.* **2013**, *49*, 10935. (c) Zhu, Y.-F.; Wei, Y.-Y. *Chem. Sci.* **2014**, *5*, 2379. (d) Niu, B.; Zhao, W.-N.; Ding, Y.-C.; Bian, Z.-G.; Pittman, C. U., Jr; Zhou, A.-H.; Ge, H.-B. *J. Org. Chem.* **2015**, *80*, 7251. (e) Dian, L.-Y.; Zhao, H.; Zhang-Negrerie, D.; Du, Y. F. *Adv. Synth. Catal.* **2016**, *358*, 2422. ³ G. A. M. Jardim, J. A. Dantas, A. A. Barboza, M. W. Paixão, M. A. B. Ferreira, *Synthesis* **2022**, *54*, 4629–4645.