

Silver Sacrificial Electrodes in Electrosynthesis: Enabling Regioselective Cyclization for Isochromenes and Dihydroisobenzofurans

Guilherme M. Martins,¹ Guilherme B. Simoso,¹ Pedro P. de Castro,² Samuel R. Mendes,³ Timothy J. Brocksom¹ and Kleber T. de Oliveira^{1*}

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

²) Department of Pharmacy, Federal University of Juiz de Fora – Campus Governador Valadares, UFJF-GV, 35010-177

³) Department of Chemistry, State University of Santa Catarina, UDESC, 89219-719

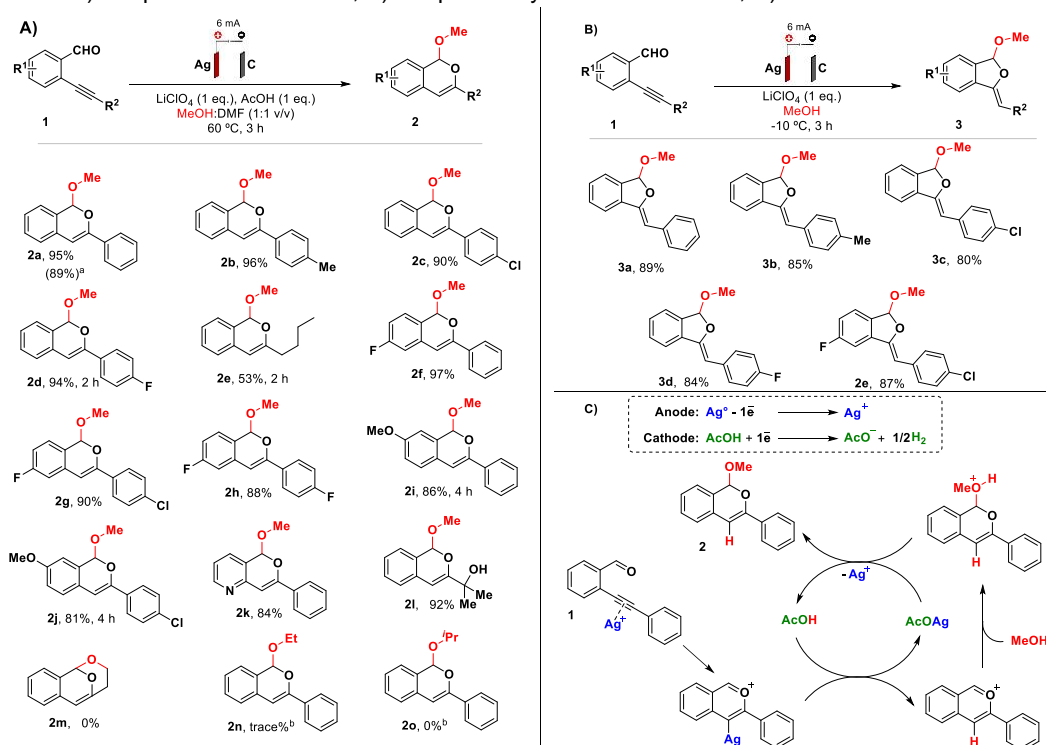
*e-mail: kleber.oliveira@ufscar.br

Keywords: Electrosynthesis, regioselective cyclization, silver.

ABSTRACT

Isochromenes and dihydroisobenzofurans are heterocycles with great importance in organic synthesis and medicinal chemistry.^{1,2} In this context, an efficient method for synthesizing isochromene and dihydroisobenzofuran analogues through electrochemical regioselective cyclization of 2-ethynylbenzaldehyde, employing silver as sacrificial electrodes is described. Remarkably, after careful optimization of the reaction conditions, the reaction presented an exceptional regioselectivity towards 5-*exo-dig* or 6-*endo-dig* cyclization, allowing the preparation of a diverse scope of products in up to 97% isolated yield (Scheme 1a and 1b), without the need for external oxidants or transition metal catalysts. The role of silver(I) and acetic acid additive in controlling the regioselectivity was investigated through control experiments and density functional theory (DFT) calculations, allowing the proposal of a plausible reaction mechanism, as shown in Scheme 1c for isochromene formation.

Scheme 1. A) Scope of isochromenes; B) Scope of dihydroisobenzofurans; C) Plausible reaction mechanism.



^a Reaction carried out using a 5 mmol scale for 22 hours at a constant current of 6 mA; ^b Using ethanol or isopropanol as solvent instead of methanol.

ACKNOWLEDGEMENTS

FAPESP (2023/04020-8, 2022/00074-3 and 2021/13924-2), FAPEMIG and FAPESC (2023TR000502).

REFERENCES

(1) *J. Org. Chem.* **2011**, 76 (22), 9548–9551. (2) *Asian J. Org. Chem.* **2022**, 11 (5), e202200012.