SEPTEMBER 23-27 2024
19BMOS
BRAZILIAN MEETING ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

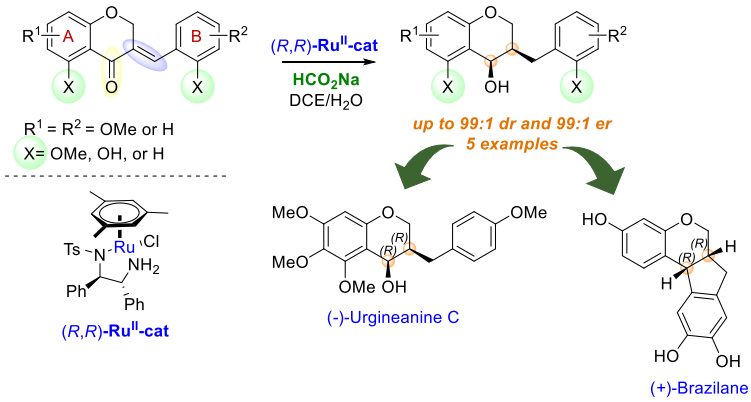
Ru(II)-Catalyzed Asymmetric Transfer Hydrogenation of Polymethoxylated 3-Arylidene Chromanones via Dynamic Kinetic Resolution.

Juliane S. Falcão, Marcos V. O. Silva, Guilherme S. Caleffi and Paulo R. R. Costa
1) Laboratório de Química Bioorgânica, Instituto de Pesquisa de Produtos Naturais Walter Mors, Universidade Federal do Rio de Janeiro, UFRJ, 21941-902, Rio de Janeiro, Brasil.
e-mail: prrcosta2011@gmail.com (PRRC); guilherme.caleffi@ippn.ufrj.br (GSC)

Keywords: *ATH-DKR, Noyori-Ikariya catalyst, ruthenium; asymmetric catalysis, hydrogen bounding*

ABSTRACT

The asymmetric transfer hydrogenation (ATH) of carbonyl compounds catalyzed by chiral transition-metal complexes is a powerful tool for obtaining key intermediates in the synthesis of optically pure pharmaceutical and natural products.[1–4] Mono-, di-, and trimethoxylated 3-arylidenechromanones at the A-ring were hydrogenated to *cis*-benzylic alcohols with high diastereomeric ratios (91:9 to 99:1) and enantiomeric excess (up to 99:1). This transformation was achieved via a one-pot reduction of the conjugated C=C and C=O bonds in the presence of 2-5 mol% of a Ru(II) chiral complex and HCO_2Na as the hydrogen source, under ATH-DKR conditions in a DCE:H_2O solvent mixture. Electronic effects (C7 and C5) and steric effects (C5) of these substituents controlled the reaction outcome. Notably, the presence of phenol groups at C5 or C2' in these 3-(benzylidene)chroman-4-ones enhanced the reaction rate, diastereo- and enantioselectivity through intramolecular hydrogen bonding. Furthermore, the oxidation of these aryl alcohols led to the enantioselective synthesis of natural homoisoflavanones with promising anticancer activities.[5,6] Additionally, the formal synthesis of the tetracyclic homoisoflavonoid (+)-brazilane was successfully accomplished.



ACKNOWLEDGEMENTS

CNPq, FAPERJ and CAPES

REFERENCES

(1) Caleffi, G. S.; Brum, J. de O. C.; Costa, A. T.; Domingos, J. L. O.; Costa, P. R. R. Asymmetric Transfer Hydrogenation of Arylidene-Substituted Chromanones and Tetralones Catalyzed by Noyori–Ikariya Ru(II) Complexes: One-Pot Reduction of C═C and C═O Bonds. *J Org Chem* **2021**, *86* (6), 4849–4858. https://doi.org/10.1021/acs.joc.0c02981.

(2) Demidoff, F. C.; Caleffi, G. S.; Figueiredo, M.; Costa, P. R. R. Ru(II)-Catalyzed Asymmetric Transfer Hydrogenation of Chalcones in Water: Application to the Enantioselective Synthesis of Flavans BW683C and Tephrowatsin E. *J Org Chem* **2022**, *87* (21), 14208–14222. https://doi.org/10.1021/acs.joc.2c01733.

(3) Gaspar, F. V.; Caleffi, G. S.; Costa-Júnior, P. C. T.; Costa, P. R. R. Enantioselective Synthesis of Isoflavanones and Pterocarpans through a Ru ^{II} -Catalyzed ATH-DKR of Isoflavones. *ChemCatChem* **2021**, *13* (24), 5097–5108. https://doi.org/10.1002/cctc.202101252.

(4) Caleffi, G. S.; Demidoff, F. C.; Nájera, C.; Costa, P. R. R. Asymmetric Hydrogenation and Transfer Hydrogenation in the Enantioselective Synthesis of Flavonoids. *Organic Chemistry Frontiers* **2022**, *9* (4), 1165–1194. https://doi.org/10.1039/D1QO01503F.

(5) Dai, Y.; Harinantenaina, L.; Brodie, P. J.; Goetz, M.; Shen, Y.; TenDyke, K.; Kingston, D. G. I. Antiproliferative Homoisoflavonoids and Bufatrienolides from *Urginea Depressa*. *J Nat Prod* **2013**, *76* (5), 865–872. https://doi.org/10.1021/np300900a.

(6) Damodar, K.; Lee, J. T.; Kim, J.-K.; Jun, J.-G. Synthesis and in Vitro Evaluation of Homoisoflavonoids as Potent Inhibitors of Nitric Oxide Production in RAW-264.7 Cells. *Bioorg Med Chem Lett* **2018**, *28* (11), 2098–2102. https://doi.org/10.1016/j.bmcl.2018.04.037.

SEPTEMBER
23-27TH
2024

19TH BMOS

BRAZILIAN MEETING
ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL