ENANTIOSELECTIVE SYNTHESIS OF BENZOPYRANE ATROPISOMERS

A. Bourhis[1], J. Rodriguez[1], D. Bonne*[1]

[1] Aix Marseille université, CNRS, Centrale Marseille, iSm2, Marseille, France

Atropisomers are of utmost interest due to their prevalence in natural products,[1] but also for their biological relevance[2] and their numerous applications as chiral materials,[3] ligands[4] and organocatalysts.[5] Among them, biaryl and heterobiaryl atropisomers are the most common ones and many synthetic approaches are available.[6] Non-biaryl atropisomers constitutes another family of these axially chiral molecules with less synthetic approaches and consequently are less represented in the literature.[7] Within this family, the highly challenging enantioselective construction benzopyrane atropisomers still constitutes a daunting challenge of modern organic synthesis.[8] Enantioselective halogenation reaction is a useful reaction for the production of atropisomers in enantioenriched form, via a dynamic kinetic resolution (DKR) of substrates presenting low enantiomerization barriers.[9] Therefore, we propose to exploit this approach for the atroposelective synthesis of axially chiral benzopyranes. While non-catalyzed version of the reaction has allowed to produce several examples of chiral benzopyranes in racemic form, encouraging enantiomeric excesses have been obtained with the use of a chiral phosphoric acid derivative and further investigations are currently undergoing in our laboratory.

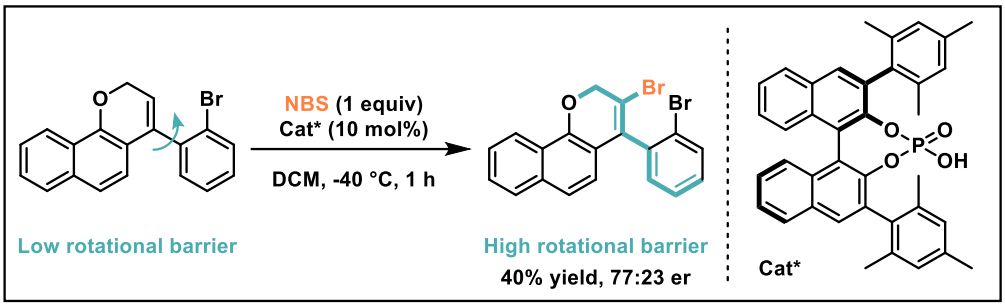

Figure 1: Bromination reaction scheme

Reference(s)

[1] N. Tajudden, D. Feineis, H. Ihmels, G. Bringmann, *Acc. Chem. Res.*, **2022**, *55*, 2370. 10.1021/acs.accounts.2c00432

[2] M. Basilaia, M. H. Chen, J. Secka, J. L. Gustafson, Atropisomerism in the Pharmaceutically Relevant Realm, *Acc. Chem. Res.*, **2022**, *55*, 2904. 10.1021/acs.accounts.2c00500

[3] B. S. L. Collins, J. C. M. Kistemaker, E. Otten, B. L. Feringa, *Nat. Chem.*, **2016**, *8*, 860. 10.1038/NCHEM.2543

[4] W. Tang, X. Zhang, *Chem. Rev.*, **2003**, *103*, 3029. 10.1021/cr020049i

[5] T. Akiyama, K. Mori, *Chem. Rev.*, **2015**, *115*, 9277. 10.1021/acs.chemrev.5b00041

[6] J. K. Cheng, S.-H. Xiang, S. Li, L. Ye, B. Tan, *Chem. Rev.*, **2021**, *121*, 4805. 10.1021/acs.chemrev.0c01306

7. E. Kumarasamy, R. Raghunathan, M.P. Sibi, J. Sivaguru, *Chem. Rev.*, **2015**, *115*, 11239. 10.1021/acs.chemrev.5b00136

[8] B-B. Gou, Y. Tang, Y.-H. Lin, L. Yu, Q.-S. Jian, H.-R. Sun, J. Chen, L. Zhou, *Angew. Chem. Int. Ed.*, **2022**, *61*, e202208174. 10.1002/anie.202208174

[9] Y. Wada, A. Matsumoto, K. Asano, S. Matsubara, *RSC Adv.*, **2019**, *9*, 31654. 10.1039/C9RA05532K