ATROPOSELECTIVE CONSTRUCTION OF AXIALLY CHIRAL 2-ARYL-PYRROLOQUINOLONES

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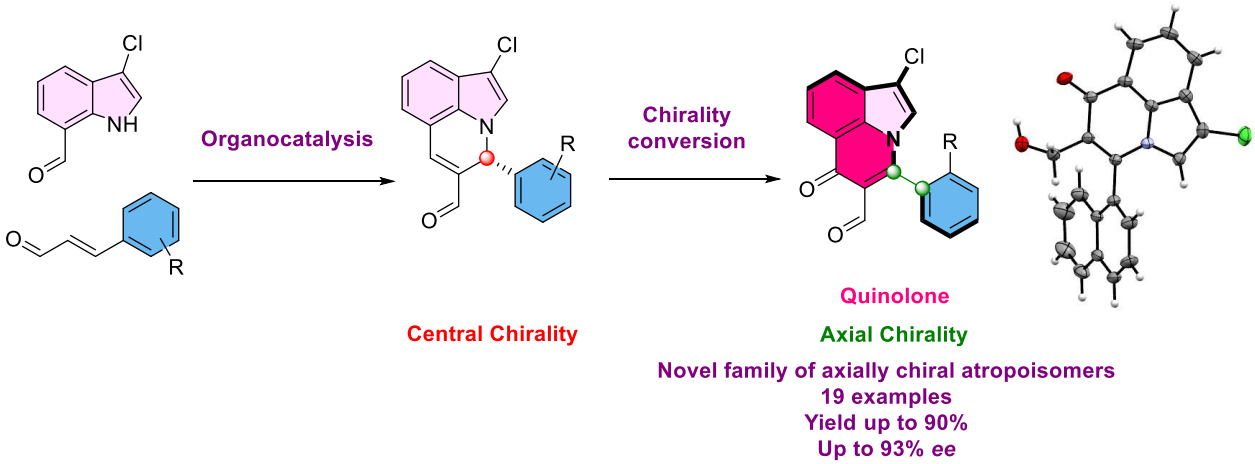
Quinolone is an important motif found in natural products and biologically relevant compounds exhibiting antibacterial[1] and anti-cancer activities.[2] Besides, 4-quinolone derivatives have found applications as ligands in metal-catalysed processes.[3] The attractive biological profile and synthetic interest have made them the centrepiece of many synthetic strategies over the past decades.[4]

While synthetic approaches have flourished recently in the literature to prepare heterobiaryl atropisomers, which represent an important class of axially chiral compounds that have stimulated the development of new synthetic approaches in the past years, the quinolone ring has never been used for making axially chiral C-C bonded aryl-heterocycle compounds.[5]

In this context, our group is focused on the atroposelective construction of axially chiral 2-aryl-pyrroloquinolones. This approach relies on a two-step protocol including an enantioselective organocatalyzed synthesis of pyrroloquinolines followed by an oxidation reaction allowed the formation of axially chiral 2-aryl-pyrroloquinolones. Thorough optimization of the experimental conditions for the second step allowed the oxygenation reaction to take place and ensured, in most cases, a central-to-axial chirality conversion with complete retention of the enantiomeric excess.[6]



References

[1] Zhang, G.-F.; Zhang, S.; Pan, B.; Liu, X.; Feng, L.-S. *Eur. J. Med. Chem.* **2018**, *143*, 710-723.
[2] Ferlin, M. G.; Chiaroletto, G.; Gasparotto, V.; Via, L. D.; Pezzi, V.; Barzon, L.; Palù, G.; Castagliuolo, I. *J. Med. Chem.* **2005**, *48*, 3417-3427.
[3] Wu, F.; Nan, C.; Ma, M.; Li, H.; Xie, J. *Appl. Organomet. Chem.* **2019**, *33*, 5195.
[4] Shen, C.; Wang, A.; Xu, J.; An, Z.; Loh, K. Y.; Zhang, P.; Liu; X. *Chem* **2019**, *5*, 1059-1107.
[5] Chen, J. K.; Xiang, S.-H.; Li, S.; Ye, L.; Tan, T. Recent Advances in Catalytic Asymmetric Construction of Atropisomers *Chem. Rev.* **2021**, 121, 4805-4902.
[6] Khlifi, T.; Jbilou, C.; Leblais, A.; Marrot, J.; Nun, P.; Ghiazza, C.; Chataigner, I.; Coeffard, C.; Moreau, X. *Org. Lett.* **2024**, *26*, *31*, 6725-6729.