Université Claude Bernard Lyon 1

Institut de Chimie et Biochimie Moléculaires et Supramoléculaires

Nouvelles variations autour de la réaction de cyclisation de Prins : application à la synthèse de tétrahydropyranes polyfonctionalisés, intermédiaires clés pour la synthèse de molécules bioactives

New variations around the Prins cyclization reaction: application to the synthesis of polyfunctionalized tetrahydropyrans, key intermediates for the synthesis of bioactive molecules

Direction: Dr Fabienne FACHE fabienne.fache@univ-lyon1.fr
Co-direction : Dr Béatrice Pelotier beatrice.pelotier@univ-lyon1.fr

The tetrahydropyran motif (THP) is present in numerous bioactive molecules. Thus, there is a need for rapid, efficient, stereocontrolled but also versatile methods to provide access to the target molecules but also to a large number of analogues.
Among the numerous strategies developed by synthetic chemists,[1] the Prins cyclization reaction has attracted a great deal of attention. Our group has successfully applied this synthetic approach to the total synthesis of natural products such as Bistramide[2] or Decytospolides A and B[3] and has also developed new applications of the Prins reaction in sequential reactions[4] or for the access to aza-derivatives.[5] Nevertheless, many scientific challenges still remain among which, the introduction of carbon nucleophiles, the use of substituted homopropargylic alcohols or substituted homoallyl amines. The access to 2,3,4,5,6-substituted THP is a challenge which also needs to be addressed. The PhD student will be in charge of the development of new methodologies to solve these issues. The results of his/her studies will be applied to the synthesis of bioactive molecules such as Mirabalin 1 (Figure 1) or to the access of analogs of anti-Alzheimer derivatives (Figure 2).

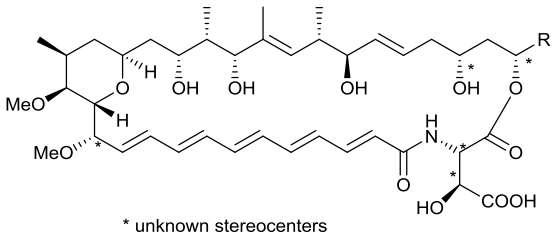

Figure 1 : THP fragment of Mirabalin 1

ICBMS UMR5246 – Université Lyon 1 – CNRS – CPE – INSA Lyon
Bâtiment Raulin/3 - 43, Bd du 11 Novembre 1918
69622 VILLEURBANNE CEDEX – France
fabienne.fache@univ-lyon1.fr
Tel : 04 72 44 85 21

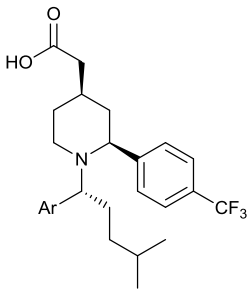

Figure 2 : Potential anti Alzheimer drugs

[1] T. Martin, J. I. Padron, V. S. Martin, *Synlett* **2014**, *25*, 12-32.

[2] L. Tomas, G. Boije af Gennäs, M.-A. Hiebel, P. Hampson, D. Gueyrard, B. Pelotier, J. Yli-Kauhaluoma, O. Piva, J. M. Lord, P. G. Goekjian. *Chem. Eur. J.* **2012**, *18*, 7452.

[3] D. Clarisse; F. Fache *Tetrahedron Lett.* **2014**, *55*, 2221-2222.

[4] D. Clarisse, B. Pelotier, O. Piva, F. Fache *Chem. Commun*. **2012**, *48*, 157; F. Fache, M. Muselli, O. Piva *Synlett* **2013**, 1781.

[5] D. Clarisse, B. Pelotier, F. Fache, *Chem. Eur. J.* **2013** *19*, 857; T. Glachet, F. Fache, B. Pelotier, O. Piva *Synthesis* **2017**, *49*, 5197.

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Tel : 04 72 44 85 21