Cascade Synthesis of Complex Polycyclic Scaffolds using Palladium Catalysis

Laboratoire d'Innovation Thérapeutique, UMR 7200 CNRS/Université de Strasbourg,
Faculté de Pharmacie, 74 route du Rhin, 67412 Illkirch, France
jean.suffert@unistra.fr http://somHet.unistra.fr

Project title: Synthesis of Cycloheptadienes by Cascade Cyclocarbopalladation: Access to New Polycyclic Scaffolds

Responsable of the project: Jean SUFFERT
Contact : jean.suffert@unistra.fr
Estimated duration: 24 mois
Funding : Frontier Research in Chemistry (FRC Foundation of Strasbourg)
Rémunération : around 2700 € brut
Early hiring date: as soon as possible
Location: Faculty of Pharmacy Strasbourg à Illkirch, UMR 7200, SOMHet Team

The candidate must have an excellent experience in organic synthesis, multi-steps synthesis, transition metal catalysis and organometallic synthesis. He (she) must possess a strong knowledge in all analytical methods routinely used in an organic chemistry laboratory.

1- Brief description of the projet :.

Natural products containing seven membered carbocycles are commonly present in the core of several compounds such as Cortistatins, Guanacastepenes or Englerins and often present interesting biological properties. The motif [5.3.0], alone is represented in more than 2500 compounds of two important families, the sesquiterpenes and the diterpenes. Another family of natural products also studied is that of guanacastepenes which show very strong antibiotic activities. However, compared to smaller rings, the synthesis of these types of polycyclic systems including a 7-membered ring is particularly difficult due to steric constraints that disadvantage cyclization and also for entropic reasons. The constant search for innovative, more efficient methods in terms of step and atom economy remains a priority for many chemists in the world because it is necessary to propose new original structures potentially able to develop important biological activities. The transition metal catalyzed carbocyclization reactions represent particularly powerful tools for accessing highly complex polycyclic systems. For several years, we have been interested in investigating new synthetic routes of various polycyclic systems containing 4, 5, 6 and 8-membered rings by cascade reactions catalyzed by palladium complexes.[1-11]

The key reaction of this methodology is based on a 4-*exo*-dig type cyclization that causes a cascade reaction sequence leading to the formation of several cycles of different sizes. It was thus possible to access very strained compounds of the cyclobutene type that eventually give, after an impressive cascade catalyzed by palladium polycyclic scaffolds containing a 7 membered ring.

2- Expected benefits : The goal of the present proposal is the development of new methodologies for a convenient access to a large collection of novel structures containing seven ring systems commonly encountered in natural product with a high potential of biological activity. These results should be published in a high impact factor journal after exemplification of the molecules prepared.

3- Significant Publications from the team domain

1. Salacz L., Girard N., Suffert J., Blond G. *Molecules*, **2019**, *24*, 595
2. Salacz L., Girard N., Blond G., Suffert J. *Org. Lett.,* **2018**, *20*, 3915
3. Blouin S., Pertschi R., Schoenfelder A., Suffert J., Blond G. *Adv. Synth. Catal.*, **2018**, *360*, 2166 **(VIP)**
4. Wagner, P ; Gulea, M ; Suffert J., Donnard, M. *Chem. Eur. J.,* **2017,** *23*, 7458
5. Blouin S., Gandon V., Blond, G. Suffert J. *Angew. Chem. Int. Ed.,* **2016,** *55*, 7208
6. T. Castanheiro, M. Donnard, M. Gulea, J. Suffert *Org. Letters,* **2014**, *16*, 3060
7. Hulot C., Blond, G., Suffert J. *Tetrahedron,* **2013***, 69,* 7568
8. Boudhar, A. Charpenay, M. Blond, G. Suffert J. *Angew. Chem. Int. Ed.,* **2013***, 52,* 12786
9. Petrignet, J. ; Boudhar, A. Blond, G. Suffert J. *Angew. Chem. Int. Ed.* **2011**, *50*, 3285
10. Hulot C., Amiri S., Blond G., Schreiner P., Suffert J. *J. Am. Chem. Soc.* **2009**, *131*, 13387
11. Hulot C., Blond G., Suffert . J. *J. Am. Chem. Soc.* **2008**, *130*, 6046 (*C&EN* **2008***, 86, 26)*