Pr Brigitte Deguin
UMR 8038 - CiTCoM
Produits Naturels Analyses et Synthèses

Evaluation report of the PhD thesis of Mr Ivaylo Momchilov SLAVCHEV entitled « Synthetic transformations of natural products ».

Following his first year of thesis at Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of sciences – laboratory "Organic synthesis and stereochemistry", Ivaylo Momchilov SLAVCHEV obtained for 3 years, a scholarship founding from the French Government to continue his studies under the frame of thesis cotutorship. So in 2015, he joined the Laboratory of Pharmacognosy and Natural Product Chemistry (UMR 8638 COMETE) of Paris Descartes University.

Professor Vladimir DIMITROV and I proposed to Mr Ivaylo Momchilov SLAVCHEV, a thesis subject concerning the use of monoterpenes commercial or not in organic synthesis. The thesis is divided into four main chapters. The first is a general introduction showing the interest of monoterpenes in fine organic chemistry. The three other chapters are related to the development of the three axes with the synthesis of series of compounds derived from three monoterpenes: (-)-fenchone, camphor and aucubin.

From the commercial (-)-fenchone a series of 31 new derivatives, bearing a cinnamic group was evaluated for their antitubercular activity against *Mycobacterium tuberculosis* $H_{37}Rv$. All compounds demonstrated significant antitubercular activity, with 4 of them matching or exceeding the potency of the referent ethambutol. The synthesis of four new arylidene and ferrocenyl-substituted derivatives of (+)-camphor were prepared and their cytotoxic and cytostatic activities were evaluated. The third axis of the thesis deals with the use of aucubin, a non-commercial natural iridoid, for the design and synthesis of new chiral ligands for asymmetric synthesis. The studies conducted from the aucubin allowed a better knowledge of the mechanistic pathways of the selective formation of 3-alkoxy-6-(pivaloyloxy)-4-(pivaloyloxymethyl)-3,3a,6,6a-tetrahydro-1*H*-cyclopenta[1,2-c]furan-1-carboxylic esters. They open new alternatives for the valorization of aucubin as a chiral scaffold. The three chapters contain a well-documented summary of the previous works, a well-argued presentation of the personal works, an experimental part proving the announced results and the bibliography.

Université Paris Descartes
Faculté de Pharmacie de Paris
4 avenue de l'Observatoire – 75006 Paris
Tél. : +33 (0)1 53 73 98 10
brigitte.deguin@parisdescartes.fr

The results obtained by Mr. Ivaylo Momchilov SLAVCHEV represent a work showing that he has acquired solid skills in the synthesis of molecules, in the study of reaction mechanisms and in structural analysis. He has also acquired solid training in the areas of biological evaluation of products of natural origin.

Due to all the elements described above, I give, as co-director, a favorable opinion to the public defense of Mr Ivaylo Momchilov SLAVCHEV for obtaining his PhD.

Paris, September 20th 2019,

Brigitte Deguin
Professor
Paris Descartes University