

Laboratoire UMR CNRS 6014 C.O.B.R.A., Université de Rouen, IRCOF, F-76821 Mont Saint Aignan Cedex. France.

Phone (work): 0033235522422, E-mail: jean-philippe.bouillon@univ-rouen.fr

EDUCATION

PhD Thesis, Organic Chemistry, Université Catholique de Louvain (Louvain-la-Neuve, Belgium).

"Synthesis and reactivity of 3-trifluoroacetylactams"
(Rhône-Poulenc Scholar, Supervisor : Pr. H.G. Viehe).

"D.E.A." (Master) in Environmental Science, Université Catholique de Louvain (Belgium).

"Licence" (diploma similar to a Honors BSc), Université Catholique de Louvain (Belgium).

"Synthesis of trifluoropropionic derivatives and of their vinyl analogs".

RESEARCH ACTIVITIES

From September 2004: **Professor in Organic Chemistry**, Rouen University, France.

March 2002: « **Habilitation à Diriger des Recherches** », Université de Reims Champagne Ardenne, France.

1996-2004: **CNRS researcher in Organic Chemistry**

UMR 6519: Réaction Sélectives et Applications, Université de Reims Champagne-Ardenne, France, Laboratory: Pr. C. Portella.

Topics: Synthesis and reactivity of bis(acylsilanes),

Mixed Fluorine and Silicon, Mixed Fluorine and Sulfur Chemistry:
synthesis of new fluorinated carbocycles and heterocycles.

1995-1996: **Postdoctoral position**, LEDSS III - Chimie recherche, Université Joseph Fourier, France, Laboratory: Dr. A. Greene.

"Total synthesis of Camptothecin".

1994-1995: **Postdoctoral position**, Institut de Chimie des Substances Naturelles, CNRS, France
Laboratory: Pr. P. Potier, Dr. J. Zhu.

"Total synthesis of new antibiotics of Vancomycine family"

CURRENT MAIN RESEARCH TOPICS

- Development of fluorinated building blocks (perfluoroketene dithioacetals, γ -ketothioesters and dithioesters) and new methodologies in Organofluorine Chemistry (Diels-Alder reactions for the synthesis of aromatic sulfides, Hetero-Diels-Alder reactions for the synthesis of dihydrothiopyrans, introduction of SF₅ substituent into nitrogen containing heterocycles).

- Synthesis of fluorinated heterocycles and their applications in Medicinal Chemistry:

- *Synthesis of mixed aminoquinolines γ -lactams and their evaluation as antimalarial agents* (collaboration: Dr. M. Médebielle, Pr. S. Picot, Lyon). Results: PCT WO n° 0132, 02/01/2011, ANR-11-EMMA-04-QUINOLAC.

- *Synthesis of pyridazino[3,4-c]quinolines and -isoquinolines as ligands of 5-HT₄ serotonergic receptors for the treatment of Alzheimer disease* (collaboration: Pr. F. Fabis, Caen).
- *Synthesis de CF₃-pyridazin-3-ones as phosphodiesterase PDE₄ inhibitors for Asthma treatment* (collaboration: Dr. S. Gérard, Reims, patent FR in preparation).

INTERNATINOAL COLLABORATION

- Institute of Organic Chemistry, Kiev, Ukraine: Synthesis of fluorinated « building blocks » and their applications.
Results: joint thesis (S. Mykaylychenko, 2005-2008), invited professor (Pr. Y. Shermolovich), more than 12 publications, 2 international research agreements.
Financial support: Rouen University, French Embassy.
- Masaryk University, Brno, Czech Republic: Synthesis of three fusionned five-membered rings via criss cross cycloaddition reactions of fluorinated allenyl azines.
Results: 5 publications, 2 Erasmus agreements.
- University Technology Brno, Czech Republic: Synthesis de tetraaryldiketopyrrolopyrrols for the development of new optics and electronics.
Results: 1 publication, 1 Erasmus agreement, invited lecturer (Dr. J. Krajkovic).
- Université de Tlemcen, Algérie: Sythesis of mixed fluorinated phenolic glycopeptides as potent anticancer agents (application Curien PHC Tassili Fundings 2015).

PhD AND POSTDOC SUPERVISION

PhD supervision: 11 thesis, 2 currently in progress (Labex SYNORG, CRUNCH)

Postdoc supervision: 3 at Reims University, 5 at Rouen University

EXTRACURRICULAR EXPERIENCE

- President of the Regional Board (Normandie Region) of the French Chemical Society.
- Member of « Grand Réseau de Recherche » (GRR Haute Normandie : Chimie Biologie Santé) et LABEX SYNORG.
- Member of the committee of the “Club Valorisation des Cyclodextrines” and “Réseau Français de Recherche en Cyclodextrines ».
- Sports: volley-ball and running (competition).

SCIENTIFIC PRODUCTION

PATENT

M. Médebielle, J.-P. Bouillon, S. Picot,

« Preparation of new 1,5-dihydropyrrol-2-one derivatives useful for the treatment of paludism and other parasitic and fungal diseases » PCT WO n° 0132, 02/01/2011, CAN: 157: 356567 ; Université Claude Bernard Lyon 1; Université de Rouen ; Hospices Civils de Lyon; Centre National de la Recherche Scientifique ; Institut National des Sciences Appliquées de Lyon.

PUBLICATIONS (2010-2014)

- 101)** E. Falkowska, F. Suzenet, P. Jubault, J. -P. Bouillon, X. Pannecoucke,
A mild and efficient synthesis of new pentafluorosulfanyl-substituted electron-deficient alkenes and allylsilanes, *Tetrahedron Lett.*, (2014), sous presse (DOI: 10.1016/j.tetlet.2014.06.117).
- 100)** F. -X. Harnisch, J. Galeta, D. Harakat, M. Potacek, J. -P. Bouillon,
Combined intra-intermolecular criss-cross cycloaddition reactions leading to perfluoroalkylated fused tricyclic nitrogen heterocycles, *J. Fluorine Chem.*, **158**, 38-43 (2014).
- 99)** M. Vala, J. Krajcovic, S. Lunak Jr., I. Ouzzane, J. -P. Bouillon, M. Weiter,
HOMO and LUMO energy levels of N,N'-dinitrophenyl-substituted polar diketopyrrolopyrroles (DPPs), *Dyes Pigment*, **106**, 136-142 (2014).
- 98)** T. Nocentini, J. -P. Bouillon, A. Capperucci, C. Portella,
Synthesis, metallation and nucleophilic reactivity of 2,6-bis(trialkylsilyl)-4H-thiopyrans, *J. Sulfur Chem.*, **34**, 692-704 (2013).
- 97)** N. Fresneau, T. Cailly, F. Fabis, J. -P. Bouillon,
Synthesis of substituted diazino[c]quinolin-5(6H)-ones, diazino[c]isoquinolin-6(5H)-ones, diazino[c]naphthyridin-6(5H)-ones and diazino[c]naphthyridin-5(6H)-ones, *Tetrahedron*, **69**, 5393-5400 (2013).
- 96)** S. Iikawa, N. Chopin, G. Pilet, J. -P. Bouillon, M. Medebielle,
Regioselective bromination of tetronic acid-derived γ -lactones and metal-catalyzed post-functionalization. An efficient access to new γ -ylidenetetronate derivatives, *Tetrahedron Lett.*, **54**, 4577-4581 (2013).
- 95)** O. S. Kanishchev, A. Lavoignat, S. Picot, M. Médebielle, J. -P. Bouillon,
New route to the 5-((arylthio- and heteroarylthio)methylene)-3-(2,2,2-trifluoroethyl)-furan-2(5H)-ones - Key intermediates in the synthesis of 4-aminoquinoline γ -lactams as potent antimalarial compounds, *Bioorg. Med. Chem. Lett.*, **23**, 6167-6171 (2013).
- 94)** O. Kanishchev, M. Sanselme, J.-P. Bouillon,
Hetero-Diels-Alder reactions of perfluoroalkyl thioamides with electron-rich 1,3-dienes: synthesis of new 2-aminosubstituted-3,6-dihydro-2H-thiopyrans and related compounds, *Tetrahedron*, **69**, 1322-1336 (2013).
- 93)** D. Cornut, H. Lemoine, O. Kanishchev, E. Okada, F. Albrieux, A. H. Beavogui, A.-L. Bienvenu, S. Picot, J.-P. Bouillon, M. Medebielle,
Incorporation of a 3-(2,2,2-trifluoroethyl)- γ -hydroxy- γ -lactam motif in the side chain of 4-aminoquinoles. Syntheses and antimalarial activities, *J. Med. Chem.*, **56**, 73-83 (2013).
- 92)** O. Stéphanie, S. Tisse, G. Coadou, J.-P. Bouillon, V. Agasse, P. Cardinael,
Influence of amino acid moiety accessibility on the chiral recognition of cyclodextrin-amino acid mixed selectors in enantioselective gas chromatography, *J. Chro. A*, **1270**, 254-261 (2012).

- 91) Z. Chai, J.-P. Bouillon, D. Cahard,
Chiral Bronsted acid-catalyzed diastereo- and enantioselective synthesis of CF₃-substituted aziridines, *Chem. Commun.*, **48**, 9471-9473 (2012).
- 90) J.-P. Bouillon, S. Mykaylychenko, S. Melissen, A. Martinez, D. Harakat, Y.G. Shermolovich,
Diels-Alder reactions of perfluoroketene dithioacetals with electron-rich 1,3-dienes: a new access to polysubstituted aromatic sulfides, *Tetrahedron*, **68**, 8663-8669 (2012).
- 89) S.A. Siriy, V.M. Timoshenko, J.-P. Bouillon,
Synthesis of polyfluoroalkyl containing thiopyran derivatives and their application in fluoroorganic chemistry, *J. Fluorine Chem.*, **137**, 6-21 (2012) (revue).
- 88) B. Plainchont, A. Martinez, S. Tisse, J.-P. Bouillon, F. Pilard, J.-M. Wieruszski, G. Lippens, D. Jeannerat, J.-M. Nuzillard,
New and old NMR experiments for the resonance assignment of complex oligosaccharides – application to a cyclodextrin derivative, *Magn. Reson. Chem.*, **49**, 781-878 (2011).
- 87) C. Brulé, J.-P. Bouillon, C. Portella,
Ethyl 3-[(ethylthio)carbonyl]-4,4,5,5,5-pentafluoropentanoate: a building block towards trifluoromethyl pyrazoles and pyrimidin-4-ones, *Synlett*, 1849-1852 (2011).
- 86) A. Lascaux, G. Delahousse, J. Ghostin, J.-P. Bouillon, I. Jabin,
Second generation calix[6]trenamides – Highly selective graftable receptors for neutral guests and contact ion pairs, *Eur. J. Org. Chem.*, 5272-5278 (2011).
- 85) T. Martin, C. Massif, N. Wermester, L. Linol, S. Tisse, P. Cardinael, G. Coquerel, J.-P. Bouillon,
Efficient preparation of enantiomerically pure α -aryl- α -trifluoromethylglycines via auto seeded programmed polythermic preferential crystallization of 5-aryl-5-trifluoromethylhydantoins, *Tetrahedron Asymmetry*, **22**, 12-21 (2011).
- 84) J. Galeta, S. Man, J.-P. Bouillon, M. Potacek,
Unexpected heterocyclic products from cycloaddition reactions of nonsymmetrical allenyl aldoketazines with substituted alkynes, *Eur. J. Org. Chem.*, 392-398 (2011).
- 83) G. Semard, V. Agasse, A. Bruchet, J.-P. Bouillon, P. Cardinael,
Convex hull: a new method to determine the separation space and to optimize operating conditions for comprehensive two-dimensional gas chromatography, *J. Chro. A*, **1217**, 5449-5454 (2010).
- 82) S. Mykhaylychenko, J.-P. Bouillon, T. Besson, Y.G. Shermolovich,
First synthesis of 2-aminosubstituted-2-perfluoroalkyl-3,6-dihydro-2H-thiopyrans by Hetero-Diels-Alder reactions of fluorinated thioamides under microwave heating, *Tetrahedron Lett.*, **51**, 990-993 (2010).
- 81) B. Plainchont, A. Martinez, S. Tisse, J.-P. Bouillon, J.-M. Wieruszski, G. Lippens, D. Jeannerat, J.-M. Nuzillard,
An alternative scheme for the multiplexed acquisition of 1D and 2D spectra, *J. Magn. Res.*, **206**, 68-73 (2010).

- 80) S. Andronati, E. Semenishyna, V. Pavlovsky, Y. Simonov, S. Makan, I. Boyko, N. Burenkova, M. Gdaniec, P. Cardianel, J.-P. Bouillon, A. Mazepa, Synthesis, Structure and Affinity of 3-alkoxy-1,2-dihydro-3H-1,4-benzodiazepin-2-ones for CNS central and peripheral benzodiazepine receptors, *Eur. J. Med. Chem.*, **45**, 1346-1351 (2010).

CHAPTER OF BOOK

- 2) G. Sépard, A. Bruchet, P. Cardinaël, V. Peulon, J.-P. Bouillon, Comparison between conventional and comprehensive GC for the search of 58 target compounds and screening of undesirable pollutants in an environmental complex matrix. In *Techneau: Safe drinking water from source to tap. State of the art & perspectives*, Van den Hoven, T.; Kazner, C., Eds. IWA: London, UK, 2009; pp 145-157.
- 1) C. Portella, J. -P. Bouillon, Perfluoroketene dithioacetals : versatile building blocks towards trifluoromethyl heterocycles, *ACS Symposium Series # 911*, Soloshonok, V. A. Ed., Oxford University Press / American Chemical Society, Washington D.C., Chapitre 12, 2005, pp 232-247.

LECTURES AND SEMINARS (2010-2014)

- C36) « Synthesis of new fused fluorinated tricyclic heterocycles and their use as ligands for 5-HT₄ serotonergic receptors », Masaryk University Brno, République Tchèque, 10 Avril 2014 (séminaire, invitation : Pr.M. Potacek).
- C35) « Synthesis, properties and applications of some monofluoro- and trifluoromethyl derivatives », Brno University Technology, République Tchèque, 09 Avril 2014 (séminaire, invitation : Pr. M. Weiter).
- C34) « Design, Synthesis and biological evaluation of fluorinated tricyclic diazine structures as ligands for 5-HT₄ serotonergic receptors », Katholieke Universiteit Leuven, Belgium, 12 Mars 2014 (séminaire, invitation : Pr. W. DeHaen).
- C33) « Novel mixed 3-(2,2,2-trifluoroethyl) aminoquinoline lactams: design, synthesis and first biological evaluation as antimalarial agents », Humboldt-Conference "Chemistry and Life", Poltava, Ukraine, 17 – 20 Mai 2013 (conférence plénière).
- C32) « Organofluorine molecules: interest, properties and few applications in medicinal chemistry », Taras Shevchenko University, Kiev, Ukraine, 1 – 16 Mai 2013 (séminaire, invitation : Pr. Z. Voitenko).
- C31) « Synthesis of nitrogen containing heterocycles based on fluorinated building blocks: an overview of Rouen's results », Technology University Brno, Czech Republic, 16 April 2013 (seminar, invitation: Dr. M. Weiter).
- C30) « Synthesis of novel 3-(2,2,2-trifluoroethyl) aminoquinoline lactams: from methodology to promising antimalarial agents application », Symposium on Chemistry and Life, Tlemcen, Algeria, 11 – 14 March 2013 (plenary lecture).

C29) « Anti-malarial drugs based on nitrogen containing heterocycles », Ukrainian State University of Technology, Dnipropetrovsk, Ukraine, 16 November 2012 (seminar, invitation: Pr. O. Kharchenko).

C28) « Mixed 7-chloro-4-aminoquinoline and γ -lactam scaffolds: design, synthesis and biological evaluation as anti-malarial agents », Taras Shevchenko University, Kiev, Ukraine, 11 November 2012 (seminar, invitation: Pr. Z. Voitenko).

C27) « Chemical optimization and biological evaluation of novel 4-aminoquinoline γ -lactam derivatives as antimalarial agents », Masaryk University Brno, Czech Republic, 26 April 2012 (seminar, invitation: Pr. M. Potacek).

C26) « Synthesis of 3-(2,2,2-trifluoroethyl)- γ -lactams: from methodology to promising antimalarial agents applications », Katolieke Universiteit Leuven, Belgium, 21 March 2012 (seminar, invitation: Pr. W. Dehaen).

C25) « Dérivés de cyclodextrines: synthèse et applications en chromatographie gazeuse énantiosélective », Université Abou Bekr Belkaid, Tlemcen, Algeria, 25 May 2011 (seminar, invitation: Pr. J. Kajima).

C24) « Cyclodextrin derivatives and enantioselective gas chromatography », Masaryk University Brno, Czech Republic, 27 April 2011 (seminar, invitation: Pr. M. Potacek).

C23) « Synthesis of trifluoromethyl nitrogen-containing heterocycles based on building blocks strategy - The example of fluorinated γ -ketothioesters », Local Czech Chemical Society, Brno, Czech Republic, 28 April 2011 (seminar, invitation: Pr. C. Mazal).

C22) « Fluorinated ketenedithioacetals and γ -ketothioesters: versatile building blocks for the synthesis of trifluoromethyl nitrogen-containing heterocycles », Katolieke Universiteit Leuven, Belgium, 03 March 2011 (seminar, invitation: Pr. W. Dehaen).

C21) « Use of γ -ketothioesters and α,β -unsaturated γ -lactones for the preparation of new trifluoromethyl heterocycles », Institute of Organic Chemistry, Kiev, Ukraine, 24 September 2010 (seminar, invitation: Pr. Y.S. Shermolovich).

TEACHING BOOK

J.-P. Bouillon, F. Estour, « QCM de Chimie Organique », Edition Ellipses (Collection PACES), 2011, ISBN : 978-2-7298-65153.