Dr. Sabrina Touchet

Associate Professor (Maître de conférences) · Organic & Therapeutic Chemistry

sabrina.touchet@univ-lorraine.fr · 06.15.06.50.98 · Université de Lorraine, Nancy

My career is characterized by significant geographical and thematic mobility. This diversity has allowed me to acquire a wide range of skills across varied fields. I holding an Engineering Degree in Chemistry from the ENSCR (*École Nationale Supérieure de Chimie de Rennes*, 2007) alongside a Master's Degree in Molecular Chemistry from the University of Rennes 1 (2007).

I subsequently obtained my PhD in Chemistry from the University of Rennes 1 in November 2010, under the supervision of Drs François Carreaux and Bertrand Carboni. This work was supported by a CIFRE fellowship funded by the company BOROCHEM and carried out within the *Institut des Sciences Chimiques de Rennes* (UMR 6226). The project aimed to develop novel synthetic pathways toward α-aminoboronic acids. To achieve this, we focused on stereoselective reactions to prepare α-aminoallylboronates from vinylboronates bearing a suitably selected functional group at the γ-position relative to the boron atom. These targets offer a dual advantage: they serve as precursors to the corresponding α-aminoboronic acids and act as highly valuable reaction intermediates in organic synthesis. My work led to the development of two novel synthetic routes: the first utilizes iridium-catalyzed allylic substitution, while the second relies on a [3,3]-sigmatropic rearrangement of allyl cyanates into isocyanates.[1]

To bridge the gap between organic chemistry and biochemistry, I completed a 3-year postdoctoral fellowship (2011–2014) in Prof. Rudolf Allemann's chemical biology group at Cardiff University (UK). My research focused on elucidating the mechanism and evolution of various terpene synthases, specifically (-)-germacrene D, (+)-α-pinene, and (+)-germacrene A synthases. This multidisciplinary project combined the multi-step synthesis of farnesyl diphosphate (FDP) analogues, their Mg^{2+}-dependent enzymatic conversion, and biochemical investigations to understand enzyme function. Moreover, the germacrene D analogues compounds were tested as alarm pheromones against aphids.[2]

I then joined the startup company AdPueriVitam (APV) for two and a half years (03/2014–08/2016). The company was located within the Faculty of Pharmacy at Université Paris-Saclay, working in collaboration with Drs Samir Messaoudi and Mouad Alami, as well as Prof. Jean-Daniel Brion from the BioCiS laboratory (*Biomolécules: Conception, Isolement, Synthèse* – UMR 8076). The project centered on the synthesis of novel heterocycles within a medicinal chemistry program involving biological and industrial partners. The goal was to develop a new drug candidate for the treatment of specific rare childhood epilepsies. In parallel, I participated in a side project focusing on palladium-catalyzed domino Heck/Buchwald-Hartwig arylations of *N*-glycosylcinnamamides.[3]

---

[1] a) Touchet, S.; Carreaux, F.; Carboni, B.; Bouillon, A.; Boucher, J.-L. Aminoboronic acids and esters: from synthetic challenges to the discovery of unique classes of enzyme inhibitors, *Chem. Soc. Rev.*, **2011**, *40*, 3895. b) Touchet, S.; Carreaux, F.; Molander, G. A.; Carboni, B.; Bouillon, A. Iridium-catalyzed allylic amination route to α-aminoboronates, *Adv. Synth. Catal.*, **2011**, *353*, 3391. c) Touchet, S.; Macé, A.; Roisnel, T.; Carreaux, F.; Bouillon, A.; Carboni, B. [3,3]-Sigmatropic rearrangement of boronated allylcyanates: a new route to α-aminoboronates and trisubstituted tetrahydrofurans, *Org. Lett.*, **2013**, *15*, 2712. d) Macé, A.; Touchet, S.; Andres, P.; Cossío, F.; Dorcet, V.; Carreaux, F.; Carboni, B. [3,3]-Sigmatropic Rearrangement/Allylboration/Cyclization Sequence: Enantioenriched Seven-Membered-Ring Carbamates and Ring Contraction to Pyrrolidines, *Angew. Chem. Int. Ed.*, **2016**, *55*, 1025 (Synfacts 2016, 12(3), 0237).

[2] a) Cascón, O.; Touchet, S.; Miller, D. J.; Gonzalez, V.; Faraldos J. A.; Allemann, R. K. Chemoenzymatic preparation of germacrene analogues, *Chem. Commun.*, **2012**, *48*, 9702. b) Gonzalez, V.; Touchet, S.; Grundy, D. J.; Faraldos, J. A.; Allemann, R. K. Evolutionary and Mechanistic Insights from the Reconstruction of α-Humulene Synthases from a Modern (+)-Germacrene A Synthase, *J. Am. Chem. Soc.*, 2014, *136*, 14505. c) Touchet, S.; Chamberlain, K.; Woodcock, C. M.; Miller, D. J.; Birkett, M. A.; Pickett, J. A.; Allemann, R. K. Novel olfactory ligands via terpene synthases, *Chem. Commun.*, **2015**, *51*, 7550.

[3] a) . Touchet, S.; Alami, M.; Messaoudi, S.; Brion, J.-D.; Galvani G.; Nous, C.; Gataullina, S.; Dulac, O. NMDA receptor modulators, compositions comprising same and use of these compounds in the treatment of diseases involving the central nervous system, Patent WO 2018224359A1

In 2016, I was appointed Associate Professor in Organic and Therapeutic Chemistry at the Faculty of Pharmacy in Nancy (Université de Lorraine). I joined the *Laboratoire Structure et Réactivité des Systèmes Moléculaires Complexes* (SRSMC, UMR 7565), which became the *Laboratoire Lorrain de Chimie Moléculaire* (L2CM, UMR 7053) in 2018. My current research focus on polar main-group organometallic chemistry, with a particular focus on the synthesis of novel heterocycles (-O, -N containing) opened up new pathways toward potentially bioactive compounds.

My research is structured around two main axes: (*i*) the development of new chiral reagents (mono-, bi-metallic, and ate complexes) for heterocycle synthesis and their functionalization via selective metallation reactions, (*ii*) the structural and mechanistic study of these novel reagents.

Developing methodologies for functionalized heterocyclic and (hetero)aromatic compounds remains crucial due to their wide-ranging applications. I have a strong interest in the synthesis of heteroaryl-lactones and heteroaryl-lactams. Existing routes to these two biologically relevant families are non-convergent and frequently rely on intramolecular cyclization, requiring highly sophisticated starting substrates that limit access to functional diversity. In this context, my efforts are directed toward developing simple, efficient, and convergent methods for the synthesis of substituted fused heterocycles and their selective functionalization. To achieve this, I employ main-group metals to perform metallation (specifically halogen-metal exchange) followed by electrophilic trapping.[4]

The key strengths of this approach include: (*i*) the development of short, efficient, and selective reaction sequences involving a reduced number of steps, thereby contributing to atom economy and minimizing the environmental impact of chemical synthesis (e.g., reducing reagent and solvent quantities, minimizing chemical waste), (*ii*) the use of abundant, cost-effective main-group metals, notably organomagnesium and organolithium reagents, but most importantly lithium organomagnesiates. These bimetallic *ate* complexes combine organomagnesium and organolithium components to yield unique, highly tunable properties.

Furthermore, I am deeply invested in the in-depth structural elucidation of these lithium organomagnesiates, both in solution and in the solid state, to better understand and predict their reactivity. This dual approach, bridging the structure and reactivity of polar organometallic complexes, remains highly underrepresented in the scientific literature.[5]

More recently, I initiated a new medicinal chemistry project aimed at designing and synthesizing a novel family of molecular pincers. This strategy focuses on utilizing small-molecule ligands with complementary donor/acceptor groups to achieve multidentate chelation of the two essential magnesium ions Mg^{2+} located within the catalytic active site of herpesvirus metalloenzymes. To guide this rational design and prioritize synthetic targets, *in silico* molecular modeling and docking studies will be integrated to optimize coordination geometries and evaluate key interactions within the catalytic pocket.

20181213 & worldwide extensions (including US, EP, JP, CA, and various European countries). b) Touchet, S.; Alami, M.; Messaoudi, S.; Brion, J.-D.; Laschet J.; Gataullina, S.; Dulac, O. Preparation of 2-quinolin-2-one derivatives, particularly indol-1-yl-1H-quinolin-2-ones and indol-3-yl-1H-quinolin-2-ones, as NMDA receptor modulators, especially NMDA antagonists, compositions including them and use of these compounds in the treatment of diseases of the central nervous system, Patent WO 2018042096A1 20180308 (with French priority FR3055331B1). c) Gataullina, S.; Galvani, G.; Touchet, S.; Nous, C.; Lemaire, E.; Laschet, J.; Chiron, C.; Dulac, O.; Dossi, E.; Brion, J.-D.; Messaoudi, S.; Alami, M.; Huberfeld, G. GluN2C selective inhibition is a target to develop new antiepileptic compounds, *Epilepsia*, **2022**, *63*, 2911. d) Luong, T. T. H.; Touchet, S.; Alami, M.; Messaoudi, S. Selective Palladium-Catalyzed Domino Heck/Buchwald-Hartwig Arylations of *N*-Glycosylcinnamamides: An Efficient Route to 4-Aryl *N*-Glycosyl Quinolin-2-ones, *Adv. Synth. Catal.*, **2017**, *359*, 1320.

[4] a) Touchet, S.; Kommidi, S. S. R.; Gros, P. C. Organomagnesiate-Promoted Enantioselective Cascade Process: Straightforward Access to Chiral 3-Substituted Isobenzofuranones, *ChemistrySelect*, **2018,** *3*, 3939. b) Touchet, S.; Yeardley, C.; O'Hara, C. T.; Gros, P. C. Critical Ligand and Salt Effects in Organomagnesiate-Promoted 3,3-Disubstituted Phthalides Synthesis from 2-Iodobenzoate Derivatives, *Eur. J. Org. Chem.*, **2021**, 4835. c) Hammas, L.; Touchet, S.; Adach, S.; Comoy, C. Organometallic Reagents: Efficient Tools for the Synthesis of Fused Pyridinyl-Lactones, *Eur. J. Org. Chem.*, **2023**, *26*, e202300800.

[5] a) Yeardley, C.; Kennedy, A.; Gros, P.; Touchet, S.; Fairley, Mclellan, M. R.; Martínez-Martínez, A.; O'Hara, C. Structural and metal–halogen exchange reactivity studies of sodium magnesiate biphenolate complexes, *Dalton Trans*, **2020**, 5257. b) *manuscript currently in preparation*.