Young Career Focus: Dr. Alexandre Gagnon (Université du Québec à Montréal, UQÀM, Canada)

BIOGRAPHICAL SKETCH

Dr. A. Gagnon

Alexandre Gagnon was born in Montréal (Canada) and studied at the Collège de Bois-de-Boulogne where he completed a Diplôme d'Études Collégiales (DEC) in natural sciences in 1993. He then obtained a B.Sc. degree from the Université de Montréal in 1996 where he conducted undergraduate research with Professors Davit Zargarian and André B. Charette as an NSERC student. In 1996, he joined the group of Professor André B. Charette as an NSERC graduate awardee to begin his doctoral work on the development of metallo-cyclopropanation reactions involving an unprecedented *gem*-dizinc carbenoid reagent. In 2001, after obtaining his Ph.D., he moved to New York, NY (USA) as an NSERC post-doctoral fellow to work on the total synthesis of xestocyclamine A under the supervision of Professor Samuel J. Danishefsky. In 2003, he started his industrial career at Boehringer Ingelheim in Laval (Canada) as a research scientist, working on the development of inhibitors of viral targets for the treatment of HIV and HCV. While at Boehringer Inglheim, he also published numerous papers on the use of tricyclopropylbismuth as a cyclopopropyl transfer agent. In 2010, he returned to the USA and joined Constellation Pharmaceuticals in Cambridge, MA, as a senior research scientist to perform research on the development of modulators of epeginetic targets. In 2011, Dr. Gagnon began his independent academic career in the chemistry department of UQÀM. His research interests lie at the interface of organic, organometallic, and medicinal chemistries. His work focuses on the development of metal-catalyzed reactions for the preparation of bioactive compounds and on the synthesis of modulators of epigenetic enzymes. He has authored more than 30 papers, trained more than 30 students and is an inventor on eight patents. His research programs are funded by the Fonds de Recherche du Québec, Nature et Technologies (FRQNT), the Natural Sciences and Engineering Research Council of Canada (NSERC), and the Canada Foundation for Innovation (CFI). He is a member of Pharmaqam and the Centre in Green Chemistry and Catalysis (CGCC) and is a member of the executive committee of the Fondation Lucien Piché.

Background and Purpose. ***SYNFORM*** will from time to time meet young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This ***SYNSTORY*** with a Young Career Focus presents Dr. Alexandre Gagnon (Université du Québec à Montréal, UQÀM, Canada).

INTERVIEW

SYNFORM | *What is the focus of your current research activity?*

Dr. A. Gagnon | My research activities are focusing on two fields: organic and medicinal chemistry. Our first research theme is centered around the development of metal-catalyzed reactions that involve organobismuthanes and that allow the introduction of highly functionalized fragments on medicinally relevant scaffolds. Our second research program deals with the preparation of modulators of epigenetic targets such as the DNA methyltransferases (named DNMTs). Epigenetics is an exciting field which studies the changes that occur on chromosomes without affecting the DNA sequence. Although this field is still in its infancy, the involvement of enzymes that perform epigenetic modifications in the development of numerous diseases is becoming clearer. Unfortunately, very few compounds that can modulate the activity of epigenetic enzymes are known, justifying research activities in that field.

SYNFORM | *When did you get interested in synthesis?*

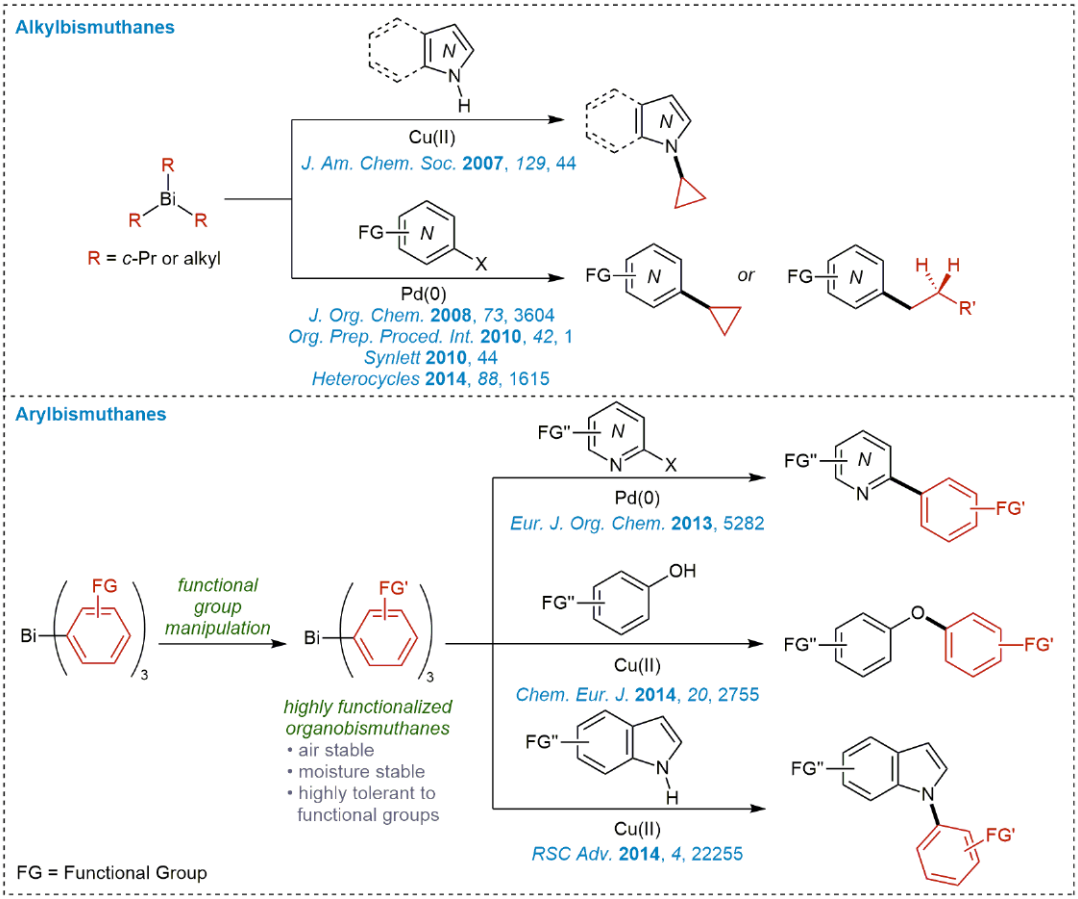
Dr. A. Gagnon | Chemistry was not my favorite subject in high school. Back then, I was more interested in mathematics and physics. My interest for this topic surfaced when I took an organic chemistry class in college given by Roger Gauthier. I was particularly attracted by the rational aspect of this science and the possibility of transforming molecules by breaking and forming new bonds. My passion for organic chemistry grew even further when I attended a course given by Professor André Charette during my first year as an

SYNFORM, 2014/12
Published online: 18.11.2014, **DOI**: 10.1055/s-0034-1379386

undergraduate student at the Université de Montréal. André was an exceptional teacher who knew how to communicate his knowledge of chemistry and his enthusiasm for science. Also, Professor Davit Zargarian, with whom I did one summer research term, was a very inspirational mentor who taught me a lot in research and who gave me an interest for organometallic chemistry. I was also extremely privileged to learn from Professor Samuel J. Danishefsky during my postdoctoral appointment and from many spectacular scientists in the industry, such as Jean-Christophe Harmange and Brian Albrecht at Constellation Pharma and Michael Bös and Paul Anderson at Boehringer Ingelheim. These are all exceptional people who had a tremendous influence on my scientific development over the years and who fuelled my desire to pursue a career in chemistry.

SYNFORM | *What do you think about the modern role and prospects of organic synthesis?*

Dr. A. Gagnon | Organic chemistry has suffered dramatically from the hurdles that the pharmaceutical industry has been facing over the past decade. As a consequence, it has become very difficult to convince the younger generation to pursue a career in this discipline. However, I firmly believe that organic chemistry is still an extremely important science that will play a major role in solving the problems that our society is and will be facing in the future. I think that we will continue to see a strong involvement of organic chemistry in many other scientific fields such as materials science, biology, medicinal chemistry and biopharmaceutical sciences. I also believe that the pendulum will swing back in the pharmaceutical industry and that there will be a larger need



Scheme 1

SYNFORM, 2014/12
Published online: 18.11.2014, **DOI**: 10.1055/s-0034-1379386

for highly competent organic chemists. In fact, we should expect a strong demand for more efficient drugs to treat diseases associated with the aging of the population. Thus, I believe that there will always be jobs for highly talented and well-trained chemists who are passionate about organic chemistry.

SYNFORM | *Your research group is active in the area of medicinal chemistry and development of new synthetic methodology. Could you tell us more about your research and its aims?*

Dr. A. Gagnon | On the medicinal chemistry front, we are collaborating with experts in academia and industry to develop modulators of various epigenetic targets.[1] As a synthetic chemistry group, we are responsible for the preparation of the molecules whereas our collaborators are taking care of the determination of their biological activities. Currently, we are mainly focusing on the synthesis of non-nucleoside inhibitors of DNMTs because the marketed drugs that target these enzymes possess a nucleoside core and thus have poor pharmacokinetic profiles. On the methodology development front, we are working on a concept that we called functional group manipulation to prepare highly functionalized organometallic reagents containing a carbon–bismuth bond. These reagents are very interesting because they are easy to prepare and because they show remarkable functional group tolerance. In addition, their reactivity depends on the oxidation state of the bismuth center, with pentavalent reagents behaving as electrophiles and trivalent counterparts reacting as nucleophiles. Using this diametrically opposite reactivity, our group has reported a portfolio of methodologies involving these reagents for the construction of C–C, C–N, and C–O bonds.[2]

SYNFORM | *What is your most important scientific achievement to date and why?*

Dr. A. Gagnon | Having spent close to ten years in the industry and only three years in academia, I believe (and I hope!) that my most important achievements lie ahead of me. However, if I were to pick one contribution to the field, I would choose the N-cyclopropylation reaction of azoles and amides involving tricyclopropylbismuth.[3] This method was the first to allow the direct transfer of a cyclopropyl group (a unit which is particularly important in medicinal chemistry) on these substrates.

Matteo Zanda

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SYNFORM, 2014/12
Published online: 18.11.2014, **DOI**: 10.1055/s-0034-1379386