2015-2016 POCC Lecture Series

December 3, 2015, 8:00 PM

Dr. L.-C. Campeau

Merck Research Labs

Discovery and Development of Novel Catalytic Reactions in the Manufacturing of Therapeutic Agents

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania

The Philadelphia Organic Chemists' Club

POCClub.org

To join us for dinner before the lecture please contact POCC's secretary Thomas Razler (thomas.razler@bms.com) at least one week ahead of time.

Originally from Cornwall, Ontario, Canada, L.-C. pursued undergraduate training in biopharmaceutical sciences at the University of Ottawa; including training in biochemistry, biology and organic chemistry. Dr. Campeau joined Merck Research Laboratories in 2007 after completing his Ph.D. in Organic Chemistry with the late Prof. Keith Fagnou, working on the discovery and development of novel direct arylation reactions during the renaissance of Pd-catalyzed C-H functionalization reactions. Since joining Merck, L.-C.'s research has been focused in the field of drug discovery and process chemistry. During his early career, he has led efforts to transition three small molecules into clinical development. One of which, Doravirine (MK-1439), an investigational drug for the treatment of HIV, is currently in Phase III clinical trials. After leading the Catalysis and Automation Laboratory from 2013-2015, where he focused on leveraging and building enabling technologies for drug discovery and development, he then accepted a position as Director of Process Chemistry, leading a group of smart creative scientists in the development of innovative chemistry to support Merck products.

Abstract: This presentation will discuss the discovery and development of novel reactions for the preparation of clinical candidate bearing an aminal stereocenter. Despite the enormous advancements of asymmetric catalysis, the catalytic enantioselective generation of acetals and related compounds was only recently demonstrated. The main enabling technology that has made this possible was the advent of chiral Brønsted acid catalysts. In the context of a drug development program, we envisioned a conceptually novel approach in which one could access aminals of type shown via the formation of a C-N bond alpha to a stereochemically labile aminal pharmacophore. The resulting indole product had a robust aminal stereocenter, therefore making it possible to dynamically resolve the chiral center. This retrosynthetic strategy was tested via high-throughput experimentation and following optimization, resulted in a reaction protocol which was demonstrated on multi-kilogram scale.