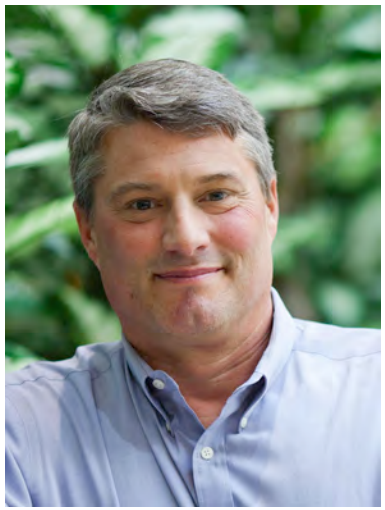

2015-2016 POCC Lecture Series

March 24, 2016, 8:00 PM

Dr. Rodney L. Parsons
Bristol-Myers Squibb

Discovery and Development of a Stereoselective Synthesis of BMS-986001: A Nucleoside Reverse Transcriptase Inhibitor (NRTI) for the Treatment of HIV Infection

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.

Dr. Rodney Parsons earned his Bachelor's Degree in chemistry in 1986 from Trinity College and then received his Ph.D. in 1992 from University of Vermont under the guidance of Professor Martin E. Kuehne. His doctoral studies were focused on development of novel routes for the construction of indole alkaloids, specifically for the total synthesis of strychnine and akuammicine. He then carried out postdoctoral studies with Professor Clayton H. Heathcock at University of California at Berkeley. While at UC Berkeley he completed the total synthesis of five marine natural products from the mirabazoles, tantazoles and thiangazole families. In 1994 he joined the Dupont-Merck Pharmaceutical Co. as a Research Scientist where he rose to the rank of Director. In 2001 he joined Bristol-Myers Squibb after the acquisition of the DuPont Pharmaceuticals Co. where he is currently an Executive Director in the Chemical and Synthesis Development Department. He has been involved with drug development programs in a number of therapeutic areas including virology, cardiovascular and metabolic diseases. His research interests include pharmaceutical process R&D, asymmetric synthesis, heterocyclic chemistry and natural products total synthesis. He has published over 40 papers and patents in these areas.

Abstract: Nucleoside Reverse Transcriptase Inhibitors (NRTI's) were first synthesized in the 1960's and have been developed as treatments for HIV over the last 30 years. BMS-986001 is an investigational nucleoside analog being developed by Bristol Myers-Squibb as a potential new treatment in this area, and development of a safe, efficient and economical process of this compound was critical to further development. Key aspects of this new synthesis include: [1] a highly diastereoselective (>20:1) cryogenic Li-acetylide addition to a ketone; [2] an efficient ring contraction of a decorated pyranose to a furanose ring; [3] a *b*-selective (>12:1) introduction of thymine at the anomeric position; and [4] pyrolysis of a rare sulfilimine intermediate to generate the dihydrofuran moiety present in the targeted structure (BMS-986001). This innovative synthetic approach provides the densely functionalized drug substance in 5 chemical steps (5 isolations) and 32% overall yield. It was discovered, developed, and executed on multi-kilogram scale from the known chiral *(S)*-benzoate BMT-916 in less than one year - leveraging simultaneous optimization and execution.