The Philadelphia Organic Chemists' Club

29th Biennial POCC Symposium and POCC Award Honoring Professor Jeffrey D. Winkler

Thursday 19 October 2006

The Connelly Center
Villanova University
Villanova, PA

PROGRAM

1:00 p.m. **Registration**, Connelly Cinema Lobby

2:00 p.m. **Prof. Robert Batey**
University of Toronto
Recent Advances in Metal Catalyzed Carbon-Heteroatom and Heterocycle Formation

3:00 p.m. **Prof. Helen Blackwell**
University of Wisconsin - Madison
Expanding the Language of Bacterial Communication Pathways with Synthetic Ligands

4:00 p.m. **Coffee Break**

4:30 p.m. **Prof. Michael Crimmins**
University of North Carolina at Chapel Hill
Strategies for the Synthesis of Medium Ring Ethers: Eunicellins to Ladder Ether Toxins

5:30 p.m. **Reception,** Villanova Room

6:30 p.m. **Banquet**, Villanova Room

8:00 p.m. **Award Address**, Villanova Room
Prof. Jeffrey Winkler
University of Pennsylvania
Synthesis of Natural and Unnatural Products

Jeffrey D. Winkler

University of Pennsylvania

Synthesis of Natural and Unnatural Products

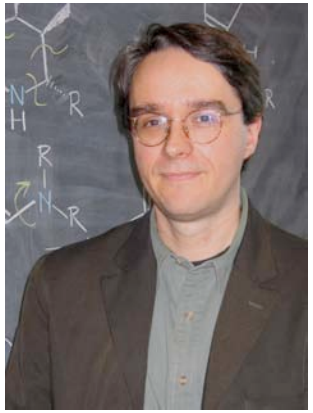
The application of the methodology developed in our laboratory to the synthesis of both naturally occurring compounds as well as designed, i.e., “unnatural” structures will be described.

Jeffrey D. Winkler was born in Chicago, Illinois on April 14, 1956. In 1973 he matriculated at Harvard College where he participated in the research programs of Professor James Wuest, Dr. Larry Blaszczak, and Professor E. J. Corey. He graduated with honors in Chemistry in 1977. In that same year, he began graduate studies at Columbia University and completed his Ph.D. degree in the laboratories of Professor Gilbert Stork in 1981. He next moved to the laboratories of Professor Ronald C. D. Breslow as an American Cancer Society Postdoctoral Fellow. In 1983, he joined the Chemistry Department at the University of Chicago as an Assistant Professor, and moved in 1990 to the University of Pennsylvania where he is currently Merriam Professor of Chemistry and a member of both the Cancer Center and the Center for Cancer Pharmacology.

His research interests have involved the development of new methodology and its application to the synthesis of structurally complex biologically active compounds, including the first total syntheses of manzamine A and ingenol. The intramolecular dioxenone and vinylogous amide photocycloaddition reactions developed in the Winkler laboratories have also been applied to the construction of mesembrine, vindorosine, perhydrohistronicotoxin, and saudin A. His honors and awards include the first American Cyanamid Young Faculty Award, the National Institutes of Health Career Development Award, a Merck Foundation Award for Faculty Development, an Alfred P. Sloan Foundation Fellowship and the Arthur C. Cope Scholar Award.

Robert A. Batey

University of Toronto



Recent Advances in Metal Catalyzed Carbon-Heteroatom and Heterocycle Formation

Nitrogen heterocycles are found in many pharmaceuticals, natural products and other biologically active compounds. New methods for the synthesis of nitrogen heterocycles are therefore both of considerable practical as well as scientific interest. During the last few years we have been interested in developing metal promoted reactions, that generate heterocycles in an efficient manner, as well as methods to generate C–N and C–O bonds that are embedded in heterocyclic structures. In this lecture, recent progress from our group toward these aims will be outlined utilizing metal promoted pericyclic, cross-coupling and C–H insertion reactions.

Rob Batey was born in England, and graduated from Oxford University with a B. A. degree in 1988. He then moved to the Imperial College of Science, Technology and Medicine in London, to work with Prof. Willie B. Motherwell, receiving a Ph.D. in 1992 on the synthetic applications of free-radical rearrangements. As a post-doctoral fellow at the University of Pennsylvania with Prof. Jeff D. Winkler, he worked on approaches toward the synthesis of taxol. Following a position at the Upjohn Company in Michigan, he joined the faculty at the University of Toronto in 1994. He is currently an Associate Professor in the Department of Chemistry, and is a scientist at the McLaughlin Centre for Molecular Medicine in Toronto.

His research interests are in the area of organic synthesis and its application to biologically interesting problems. His research program encompasses the development of new organic reactions, catalysis, organoboron chemistry, the synthesis of alkaloid natural products and other heterocycles, and their application in probing cellular processes and as anticancer agents. His work has been recognized through several awards including the Merck-Frosst Centre for Therapeutic Research Award (2006), Merck Academic Development Program Award (2005), Premier's Research Excellence Award (2000), the Bio-Méga/Boehringer Ingelheim Young Investigator Award for Organic Chemistry (1998) and the Canadian Society of Chemistry / Astra Pharma Award (1997).

Helen Blackwell

University of Wisconsin - Madison

Expanding the Language of Bacterial Communication with Synthetic Ligands

The broad goal of our research is the design, synthesis, and evaluation of new chemical inducers that modulate cell-cell communication mechanisms in bacteria. The ability of bacteria to communicate with themselves and function as a group is central in the development of infectious disease. Gram-negative bacteria use a chemical 'language' of small molecules (or autoinducers) and their cognate protein receptors to sense their local population density in a phenomenon known as 'quorum sensing'. At high population densities, pathogenic bacteria use this sensing mechanism to organize into structured communities called biofilms and activate virulence pathways that are the basis for myriad chronic infections. The development of methods to control bacterial quorum sensing and attenuate biofilm formation would have a major impact on human health. We reasoned that synthetic ligands could be used to intercept bacterial autoinducer/receptor binding and modulate quorum sensing and biofilm formation. We recently validated this approach through the discovery of a set of the most potent quorum sensing antagonists and agonists known. This talk will present our on-going work in this area.

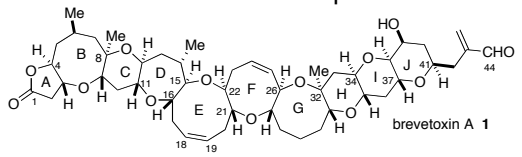
Helen Blackwell was born in Cleveland, Ohio and attended Oberlin College for her undergraduate studies, graduating with highest honors in chemistry in 1994. She pursued her graduate studies in organic chemistry at the California Institute of Technology with Professor Robert Grubbs. Helen received her Ph.D. in 1999 and then spent three years as Jane Coffin Childs postdoctoral fellow in the lab of Professor Stuart Schreiber at Harvard University. In 2002, she joined the faculty of the University of Wisconsin-Madison, where she is presently an Assistant Professor of Chemistry. Her main research interests are the development of new synthetic organic chemistry methods and their application to design molecular tools to ask important questions in bacteriology and ecology. Helen is the recipient of a Shaw Scientist Award of the Greater Milwaukee Foundation (2004), an NSF CAREER Award (2005), a Research Corporation Cottrell Scholar Award (2005), and a Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease Award (2006). She was selected as a MIT Technology Review Top 35 Innovator under the Age of 35 in the US (2005) and as an Alfred P. Sloan Foundation Fellow (2006).

Michael T. Crimmins

University of North Carolina at Chapel Hill

Strategies for the Synthesis of Medium Ring Ethers: Eunicellins to Ladder Ether Toxins

Ladder ether toxins such as the brevetoxins A and B, the ciguatoxins, and the gambieric acids which are produced by algal blooms of marine dinoflagellates can have devastating effects on marine life. The most potent toxin produced by *Gymnodynium breve* Davis is brevetoxin A (**1**). It is reportedly lethal to zebra fish at 3 parts per billion. Our previous work on the Laurencia and octocoral metabolites have led to strategic advances in methods for the construction of medium ring ethers. Recently, we initiated a program toward the total synthesis of brevetoxin A, which exploits many of these strategic developments. Details on the development of strategies for synthesis of medium ring ethers and progress toward a highly convergent synthesis of brevetoxin A will be presented.



Michael Crimmins was born in E. St. Louis, Illinois on January 3, 1954. He received his B.A. degree from Hendrix College (1976), his Ph.D. from Duke Univeristy under S. W. Baldwin (1980) and was a postdoctoral associate at California Institute of Technology with D. A. Evans from 1980-81. He became Assistant Professor at the University of North Carolina at Chapel Hill in 1981, was promoted to Associate Professor (1988) and then Professor (1993). In 2001 he was named George and Alice Welsh Distinguished Term Professor and assumed the position of Mary Ann Smith Distinguished Professor in 2003.

Professor Crimmins' research interests are in the development of new synthetic methods and their application to the total synthesis of biologically active compounds. A variety of new synthetic methods have been developed in his laboratories and his research group has completed the total synthesis of a wide variety of structural types of natural products.

Professor Crimmins' research has been recognized by an Alfred P. Sloan Foundation Fellowship in 1986 and an American Cyanamid Faculty Fellowship in 1994. He received an Arthur C. Cope Scholar Award in 2001 and the Charles H. Herty Medal from the Georgia Section of the American Chemical Society in 2004. In addition, he was recognized with the Tanner Faculty Award for Excellence in Undergraduate teaching in 1999. He is a member of the Editorial Advisory Board of the *Journal of Organic Chemistry* and the scientific advisory board of Chimerix, Inc.

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About POCC: Founded more than sixty years ago, The Philadelphia Organic Chemists' Club is one of the oldest independent chemistry clubs in the United States. Its central purpose is to facilitate interaction between scientists from academia and the many chemical and pharmaceutical companies in the greater Philadelphia area. Information about the POCC, its officers, membership, and seminar schedules for Fall 2006 and Spring 2007 can be found at:

http://www.chem.temple.edu/main/Pocc/default2.htm