DEPARTMENTS OF CHEMISTRY
Seminar Series

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GSB 307

Iterative Cyclization Strategies for the Synthesis of Polycyclic Targets

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The development of new iterative cyclization strategies for rapid assembly of complex molecules will be described. These strategies have arisen from our work on the halo-Nazarov electrocyclization, a cationic process that occurs diastereospecifically. The reaction cascades combine *halo*-alkynyl Prins coupling, followed by different variants of the *halo*-Nazarov cyclization, and involve a series of cationic intermediates. The cationic cascades resemble classical polyene cyclization, but follow irregular patterns to deliver a variety of densely functionalized scaffolds in one or two steps. A range of fused and spirocyclic ring systems can be accessed, containing functionalized cyclopentanes, oxygen and nitrogen heterocycles, and a vinyl halide synthetic handle. The sequences are highly diastereoselective, and can produce enantiopure adducts. The strategy has been applied successfully to the total synthesis of tubingensin A.

Strategically, the method couples two simple precursors: an enyne/ arenyne and the carbonyl derivative that serves as the initiating carbon. The initiating carbon can be an aldehyde, ketone, imine, *N,O*-acetal, acetal, ketal or enol ether, and subsequent iterative cyclization converts the initiating carbon into an sp^3 center within a polycyclic framework.

Professor Alison J. Frontier

Professor Frontier grew up in suburban Detroit, and received her AB from Harvard in 1992, where she did undergraduate research with Prof. Yoshito Kishi. Immediately after graduation, she took a two-year position as an Associate Chemist at the Merck Research Laboratories at Rahway, NJ, after which she pursued graduate studies at Columbia University with Samuel Danishefsky, earning her PhD in 1999. She was awarded a National Institutes of Health Postdoctoral Fellowship to work with Barry Trost at Stanford University. In 2002 she accepted a faculty position at the University of Rochester, where she is now Professor of Chemistry.

Her research interests focus on synthetic organic chemistry, and has active projects in both target synthesis and method development. Students in her research group are pursuing novel strategies for the synthesis of bioactive, structurally interesting natural products, as well as the development of pericyclic reactions and multistep cationic cyclization cascades. In particular, her group has developed several new variants of the Nazarov electrocyclization, including Nazarov cyclization/ Wagner-Meerwein rearrangement sequences, cyclizations initiated by allenol ether oxidation and conjugate addition, and *halo*-Nazarov cyclizations. Recent investigations leverage alkynyl Prins reactions to effect double annulation processes.

In 2004 she launched "Not Voodoo," a website designed to help students who are beginning independent experimentation for organic chemistry research projects. The site attracts hundreds of visitors each day from research laboratories around the world. In 2015 she pioneered a novel course for undergraduates entitled "The Chemistry of Poisons," which combines advanced organic chemistry, history, mythology and popular culture.