PHILADELPHIA ORGANIC CHEMISTS' CLUB

DATE: Thursday, May 29 th , 2003; 5:00 pm Cocktail and dinner; 8:00 pm seminar

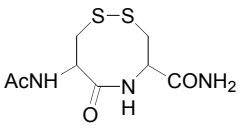
PLACE: Room 102, New Chemistry Building, University of Pennsylvania, 34th and Spruce Streets, Philadelphia, PA

SPEAKER: Allen B. Reitz, Ph.D., Johnson and Johnson Pharmaceutical R&D

Allen Reitz attended University of California schools, receiving a Ph.D. in Chemisty with Murray Goodman at UC, San Diego. He then worked with Bruce Maryanoff at McNeil Pharmaceutical, a subsidiary of Johnson & Johnson, in Spring House, Pa. Remaining at JNJ, he is now the Central Nervous System (CNS) Chemistry Team Leader and a Senior Research Fellow. His research lies in the treatment of neurological and psychiatric disorders, based on the interplay of synthesis, conformational analysis, function, and design. He invented 3 compounds that are in human clinical trials. Allen now has 92 publications and 26 issued U.S. patents, and the dubious distinction of being an author (along with Ellen Baxter) of the longest *Organic Reactions* volume written to date ("Reduction Aminations with Borohydride and Borane Reducing Agents", vol. 59, 2002). He is Editor-in-Chief of *Current Topics in Medicinal Chemistry* and an editor of the continuing book series *Frontiers in Medicinal Chemistry*. He has received the Philip B. Hofmann Research Scientist Award (1994) and the Corporate Office of Science and Technology Excellence in Science Award (1999).

TITLE: **"Novel Scaffolds and β-Turns that mimic ox-[Cys-Cys]: Design, Synthesis and Conformational Analysis"**

ABSTRACT: We have investigated the use of the ring-closing metathesis (RCM) and Bergmann cyclization reactions to prepare novel scaffolds that establish pendent groups in a defined geometry for understanding the relationship of structure and function. Our initial target is the unusual oxidized eight-membered-ring disulfide ox-[Cys-Cys] (**1**) found in the N-terminal extracellular domain of most nAChR subtypes. A thorough conformational analysis performed on **1** indicates that it exists as a mixture of four distinct conformers in water (47:15:29:9), and that the major one (T^-) is a type VIII □-turn. We have prepared all of the possible stereoisomers of both the unsaturated and saturated lactams **2** using an RCM-based strategy, and have examined them in both water and the solid state. The 2*S*,7*S* diastereomer of **2** is type VIa β-turn, and the 2*S*,7*S* isomer is very similar to the C^+ conformation of **1**. We have applied the Bergmann cyclization to substrate **3**, which may allow for the incorporation of enediynes into expanded sequences that can specifically cleave either defined regions of DNA or protein targets.



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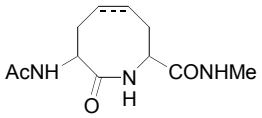

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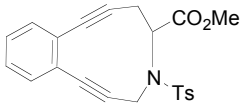

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DINNER: The meeting will be preceded by cocktail and dinner starting at 5:00 pm at The Palladium Restaurant & Bar, 3601 Locust Walk.

Reservations should be made by calling Celine Duquenne at (610) 917-5120 or by e-mail at Celine.Duquenne@gsk.com **before 5:00 pm, Thursday, May 22th, 2003. Please pay the $40.00 for dinner when you attend. Thank you.**