2007-2008 POCC Lecture Series

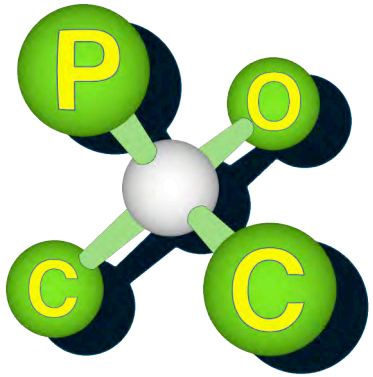
December 13th, 2007, 8:00 PM

Prof. Jacquelyn Gervay-Hague

University of California Davis

Bio-Inspired Iodides, Sulfones, and Scaffolds

Carolyn Hoff Lynch Lecture Hall
Chemistry Building, University of Pennsylvania



Biography: Prof. Gervay-Hague received her B.S. degree in 1985 from UCLA, and her Ph.D. in 1990 also from UCLA under the direction of Prof. M. Jung. After a NIH postdoctoral fellowship at Yale University with Prof. S. Danishefsky she began her independent career in 1992 at the University of Arizona as Assistant Professor and in 1998 she was promoted to Associate Professor. In 2001 Prof. Gervay-Hague was appointed Professor of Chemistry at the University of California, Davis. Her research interests are in the area of carbohydrate chemistry directed toward the design and synthesis of chemotherapeutics targeting HIV infection and cancer. She has received many awards and is currently an associate editor of the *Journal of Organic Chemistry.*

Abstract: The synthesis of alpha-galactosyl ceramide natural products is a core area of investigation in the Gervay-Hague lab. These natural products were originally isolated from marine sponge, and quantities for biological studies were scarce. One-pot synthetic routes for large quantity production of alpha-galactosyl ceramides using glycosyl iodide chemistry have been developed. Our laboratory is a leader in developing these methods, which exploit the unique reactivity of glycosyl iodides providing highly efficient routes to important synthetic precursors for natural product synthesis and combinatorial library construction.

A second key area of investigation includes the use of sulfones as neutral phosphate isosteres. We have recently reported detailed studies of a new class of HIV-integrase inhibitors having a geminal-disulfone functionality with potent antiviral selectivity. Computational studies suggest that two major modes of binding are likely and that the disulfone analogs bind similarly to previously identified HIV-IN inhibitors currently in clinical trials. A compound capable of direct inactivation of HIV has also been identified.[1]

Finally, we have begun a new area of investigation focused on developing methods for the efficient conjugation of site-specific functionalized proteins that are used for cancer chemotherapeutics. In an effort to improve avidity, singly functionalized scFv proteins directed against the MUC-1 antigen have been successfully dimerized using a 1-3 dipolar cyclization strategy. Our central contributions involve introduction of a trialkyne functionality onto rigid scaffolds that promote the cyclization process.

[1] Duong, Y.T.; Meadows, D.C.; Srivastava, I.K.; Gervay-Hague, J.; North, T.W. "Direct Inactivation of Human Immunodeficiency Virus Type 1 by a Novel Small-Molecule Entry Inhibitor, DCM205." *Antimicrob. Agent Chemother.*, **2007**, *51*, 1780-1786.