



# 2011-2012 POCC Lecture Series

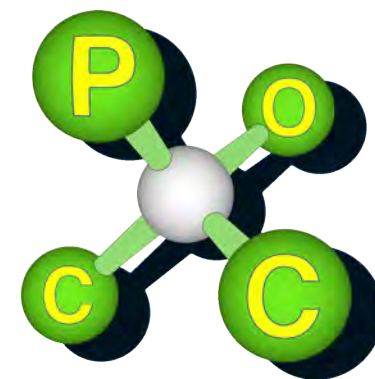
October 27, 2011, 8:00 PM  
≈ Allan R. Day Awardee ≈

Prof. Douglass F. Taber  
University of Delaware

## Computational Organometallic Chemistry: Synthesis of (-)-Veratramine

Carolyn Hoff Lynch Lecture Hall  
Chemistry Building, University of Pennsylvania

The Philadelphia  
Organic Chemist's  
Club



POCClub.org

Douglass F. Taber was born November 11, 1948 in Berkeley, California. He earned a B.S. in Chemistry with Honors from Stanford University in 1970, and Ph.D. in Organic Chemistry from Columbia University in 1974 (G. Stork). After a postdoctoral year at the University of Wisconsin (B.M. Trost), Taber accepted a faculty position at Vanderbilt University. He moved to the University of Delaware of Delaware in 1982, where he is currently Professor of Chemistry (<http://valhalla.chem.udel.edu>). Taber is the author of more than 200 research papers on organic synthesis and organometallic chemistry. He is also the author of the weekly Organic Highlights published at <http://www.organic-chemistry.org/>

**Abstract:** The Hedgehog (Hh) signaling pathway regulates patterning and progenitor cell fates during fetal development. In mammals, three Hh ligands (sonic, Indian, and desert) mediate signaling of this pathway. Without the Hh ligand, the receptor patched (Ptch1) blocks Hh signaling through catalytic inhibition of smoothened (Smo), a transmembrane protein that is the next link in Hh pathway activation. Activation of Smo leads to activation of the Gli transcription factors that trigger the Hh transcriptional program, including up-regulation of Ptch1 and Gli1 expression. The *Veratrum* alkaloids veratramine **5** and cyclopamine **6** are Hh pathway antagonists, that act directly on Smo. We will describe the first modern-day total synthesis of a *Veratrum* alkaloid, (-)-veratramine **5**, and progress toward the synthesis of (-)-cyclopamine **6**. The absolute configuration of the precursor **4** was set by enantioselective allylation of the prochiral enone **1**.

