UCLA Chemistry & Biochemistry

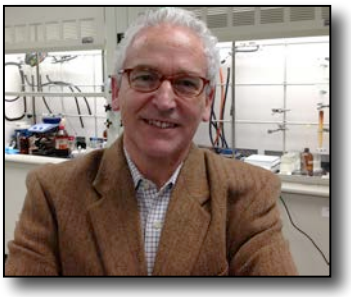
Procter&Gamble

presents

UCLA Student Organization for Cultural Diversity in Science Lectureship Series

with

Professor Gerald B. Hammond



Department of Chemistry
University of Louisville

"The Taming of the Shrew: Recent Advances in Nucleophilic Fluorination"

Abstract. In the majority of fluorine-containing therapeutic drugs, it is the metabolic stability of the C-F bond what motivates the pursuit of fluorine replacement strategies. And in the vast majority of these cases, it is the aromatic C-F bond or the aromatic CF_3 group what matters most to medicinal chemists. Therefore, with few exceptions, the biochemical space of fluorine has been limited to mostly aromatic or heteroaromatic substitutions. Our efforts to expand the medicinal space of organofluorine compounds led to the discovery of a difluoropropargyl-containing small molecule (XB05), with potent antiproliferative and cytotoxic activities.

The problem of increasing the structural diversity of organofluorine compounds lies in the difficulty of handling fluorine. Most, if not all, fluorinating reagents (electrophilic or nucleophilic) are made from hydrogen fluoride (HF) but HF itself is a hazardous gas at room temperature and is very difficult to handle. Chemists have previously controlled the reactivity of HF forming hydrogen-bonded complexes using organic molecules such as pyridine and triethylamine, but these organic bases reduce the acidity of the system and interfere with many metal catalysts.

Using the concept of hydrogen-bond basicity, developed by Laurence, we selected DMPU to stabilize HF through hydrogen bonding. DMPU (pK_{BHX} = 2.82) is a better hydrogen bonding acceptor than pyridine (pK_{BHX} = 1.86) and Et_3N (pK_{BHX} = 1.98) but it is much less basic than pyridine and Et_3N; in addition, DMPU is weakly coordinating toward metals. We have recently reported that this DMPU-HF complex is not only easy to handle but also it is an efficient fluorination system for the regioselective mono- and di-hydrofluorination of alkynes and other ring opening and ring forming reactions. Recent advances on the properties and reactivities of HF-DMPU and other designer HF-based complexes will be presented.

Friday, April 7, 2017

1:30 PM

Cram Conference Room – 3440 Molecular Sciences Bldg

For further information, contact David Gingrich at gingrich@chem.ucla.edu