Wednesday, February 23, 2022
4:00 P.M.

Ackert Hall, Room 120

Biochemistry & Molecular Biophysics **Seminar**

Simplicity as the Driving Force for New Reaction Invention: Adventures in Organofluorine Chemistry and Catalysis

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Due to their unique properties organofluorine compounds occupy a privileged role in the areas of synthetic organic, materials and biological sciences. It has been recognized that installation of fluorine or fluoroalkyl (—R_F) groups into organic molecules often imparts exceedingly important and unique biological and physicochemical properties. Accordingly, organofluorine compounds are known to exhibit superior metabolic stability, binding affinity, membrane permeability, and enhanced pharmacokinetic profiles in some instances. Thus, significant attention has been devoted to design new synthetic methods for these compounds. Consequently, more than 20% of newly approved pharmaceuticals and approximately 40% of registered agrochemicals possess one or more fluorine atoms. In this context, the trifluoromethyl (–CF_3) and difluoromethyl (–CF_2H) groups are valuable moieties for tuning the lipophilicity and bioavailability of drug-like molecules resulting in a high prevalence in agrochemicals and active pharmaceutical ingredients (APIs).

In this context, our group in currently engaged in the development of direct and catalytic transformations of carboxylic acids feedstocks. Multiple deoxygenative transformations of these readily available starting materials giving rise to fluoroalkyl (–CF_3, –CF_2H) ketones, aldehydes and acyl fluorides directly, will be delineated. Key to the success of these transformations is the use of *acyloxyphosphonium ions* as acyl electrophiles, readily and conveniently prepared *in-situ* from the parent carboxylic acids and commodity chemicals. Notably, the transformations proceed under mild conditions in short reaction times and exhibit excellent chemoselectivity and functional group compatibility. Late-stage functionalization of active pharmaceutical ingredients (APIs) utilizing our approach will be also discussed.