Making, Breaking, and Using C-F Bonds

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This presentation will be divided in two parts.

The first one will focus on the use of fluoride as a leaving group. Typically, fluoride has the worst leaving group ability of the halogen series in nucleophilic substitution reactions on alkyl halides. It is therefore not surprising that reactions involving the use of fluoride as a leaving group on a sp^3 carbon are uncommon. I will present a series of synthetic transformations involving the use of a C(sp^3)-F bond activation as a key step. In particular, nucleophilic substitution reactions of activated alkyl fluorides in aqueous solvent or using a triol activator will be discussed. Finally, we will examine the effect of stronger hydrogen-bond donor solvents on the reaction pathway. As such, reactions of benzylic fluorides in Friedel-Crafts reactions will be presented.

Understanding the interactions between lipid membranes and small molecules, peptides or proteins is of primary importance to determine their mechanism of action. In this context, solid-state NMR is a method of choice to study their effects on model membranes. Our goal involves marking, with a fluorine atom, phosphoglycerolipids to mimic eukaryotic and prokaryotic cell membranes. In this second part, the synthesis and characterization of monofluorinated dimyristoylphosphatidylcholine derivatives (F-DMPC) will be presented. Biophysical studies using infrared spectroscopy and solid-state NMR suggest that the incorporation of monofluorinated analogs of DMPC in model membranes does not significantly perturb the properties of the lipid bilayers.