UNIVERSITY OF RHODE ISLAND
Department of Chemistry
SEMINAR

3:00 P.M., Monday, April 15, 2024
Room 105 – Beaupre Center

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University of Minnesota

Inspiration from Fluorination: Using Fluorinated Biomolecules for Imaging and Drug Development

HOST

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Fluorine is the thirteenth most abundant element in the earth's crust and most abundant halogen, but remains largely absent from nature's most essential biopolymers and natural products. Despite this absence in biology, organofluorine compounds hold significant promise for impacting human health, including for imaging applications (^{18}F PET and ^{19}F MRI), structural biology, drug screening, and drug development. As one innovation in our lab, we develop protein-observed ^{19}F NMR (PrOF NMR) approaches using ^{19}F-labeled protein side-chains that are enriched at protein-protein-interaction interfaces. We use PrOF NMR for characterizing protein-protein, nucleic acid interactions, and drug discovery applications.

Today, I will discuss a medicinal chemistry application of PrOF NMR, which has led to potent inhibitors of a class of proteins called BET bromodomain-containing proteins, including BRD4 in the first part of the talk. BET proteins are emerging drug targets for developing anticancer and anti-inflammatory agents. I will present how we have used PrOF NMR to drive a medicinal chemistry project to develop highly selective inhibitors for both anticancer applications in multiple myeloma, as well as a new therapeutic approach for inflammatory liver disease. In the second part of the talk, using a ^{19}F NMR-based structure-property study of synthetic organofluorine molecules, this research led to the development of new organofluorine liquids with improved temperature responsiveness, high signal, and reduced non-magnetically equivalent fluorine resonances. Environmental degradation analysis using reverse-phase HPLC and quantitative ^{19}F NMR demonstrates a rapid degradation profile mediated via the arylfluorine core of the temperature sensors to avoid environmental persistence concerns encountered by other highly fluorinated molecules. Additional efforts towards designing new oximetry agents and molecular imaging agents, using fluorinated synthetic peptides will also be described.