

## Lanny Liebeskind Cope Scholar Award Symposium II

**Sponsor:** Johnson and Johnson, Merck, ACS Division of Organic Chemistry

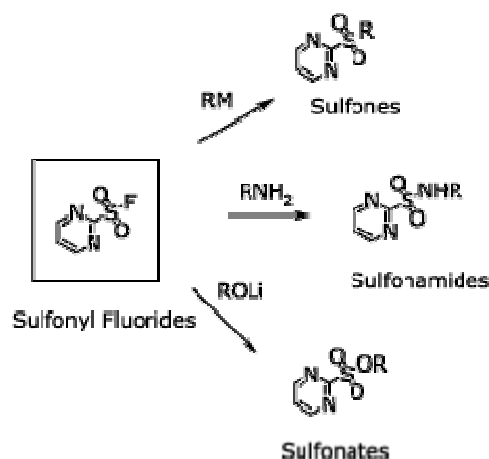
**Organizer:** Dr. Mark E. Welker Wake Forest University, Winston-Salem, NC

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### 222. Sulfonyl Fluorides: Stable Sulfonyl Chloride Surrogates

**Gary D. Allred**, Synthonix Corporation, Wake Forest, NC

Although sulfonyl chlorides are important and powerful building blocks, there are few commercially available heterocyclic sulfonyl chlorides. This is because many heterocyclic sulfonyl chlorides are thermally unstable. When the sulfonyl chloride group is adjacent to a heteroatom, extrusion of sulfur dioxide occurs with concomitant formation of the aryl chloride. Thus, most heterocyclic sulfonyl chlorides must be generated in situ at low temperature and reacted immediately. Sulfonyl fluorides have been found to be shelf-stable and reactive surrogates of sulfonyl chlorides. This presentation details the synthesis, stability, and reactions of heterocyclic sulfonyl fluorides.



### 223. Correlating SAR Trends with Crystallographic Data in a Series of Cathepsin S Inhibitors

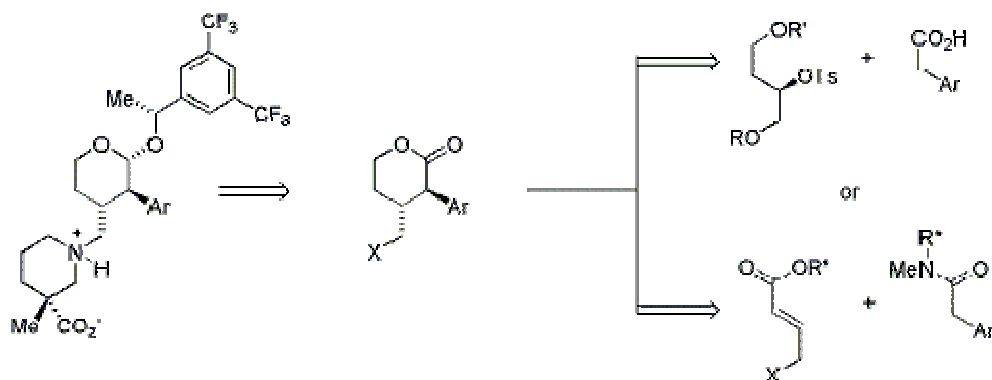
**James P. Edwards**, Johnson & Johnson Pharmaceutical Research and Development, LLC, San Diego, CA

We have previously disclosed several closely related series of cathepsin S inhibitors based upon a bicyclic pyrazole core structure. Although clear SAR trends were evident from examination of the enzymatic data of diverse structures, a comprehensive understanding of the mode of binding of these molecules to the target protein awaited structure determination via X-ray crystallographic analysis. In this presentation will be described the SAR of these inhibitors in the context of the key interactions observed in several co-crystal structures. The novel binding mode of these noncovalent cathepsin S will be compared to previously reported structures of inhibitors covalently-bound to cathepsin S, and the ramifications of these differences to drug design discussed.

### 224. Synthesis of Tetrahydropyran NK1 Receptor Antagonists

**Mark A. Huffman**, Merck and Co., Inc., Rahway, NJ

Three practical asymmetric routes were developed to synthesize tetrahydropyran-containing NK-1 receptor antagonists. The first route sets the core stereochemistry through stereospecific enolate alkylation with a chiral 2° alkyl sulfonate. The second and third generation syntheses employ asymmetric conjugate addition to  $\alpha,\beta$ -unsaturated esters using amides of the chiral auxiliary pseudoephedrine.



## 225. Synthesis and Tandem Reactions of Main Group Element Boron, Aluminum and Silicon Substituted 1,3-Dienes

**Dr. Mark E. Welker**, Ramakrishna Pidaparathi, Subhasis De, Ken Crook and John Solano, Wake Forest University, Winston-Salem, NC

We will report the preparation of some boron, silicon and aluminum-substituted dienes. We will then report palladium catalyzed tandem Diels-Alder/Cross-Coupling Reactions of these main group-substituted Dienes. We will also report rhodium catalyzed Diels-Alder/hydrolysis reactions which utilize boron diene starting materials.

## 226. Seeking Novel Reactivity and Selectivity in Organic Synthesis

**Lanny S. Liebeskind**, Emory University, Atlanta, GA

This lecture will describe the development of novel methods for carbon-carbon and carbon-heteroatom bond formation that occur between functionally-rich thioorganic substrates and boronic acids (and organostannanes) under non-basic reaction conditions at ambient temperatures. Templating with redox-active, thiophilic metal catalysts plays a key role in these site-specific transformations. Recent progress in the development of two new systems will be presented: (1) reaction systems that require only catalytic quantities of thiophilic metal catalysts, some of which function under aerobic conditions, and (2) conceptually related and synthetically novel transformations of N-O substrates.