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Editorial

Editorial for special issue of JFC on Biomedicinal Chemistry

The development of new reagents for efficient fluorination of a wide variety of substrates combined with new concepts of drug design and the expanding list of biological targets evolving from genomics and proteomics insure an increasingly important role of fluorine in drug development. Aided by new synthetic tools, chemists have produced a large inventory of fluorinated agents for biomedicinal applications. Much early research was characterized by a rational approach based on the known special properties of fluorine. Successes were impressive in number and in concept. More recently, an empirical flavor has been gaining importance. This has accompanied the advent of new strategies in drug discovery that include high throughput screening and combinatorial and parallel syntheses. Fluorine, trifluoromethyl groups, and other fluorinated species are routinely explored as substituents in drug optimization studies. While these substitutions are based on well-founded principals of medicinal chemistry, the mechanism of any fluorine-induced improvement of drug properties may not be addressed until after biological results are examined. The results of these studies indeed can and do add to the knowledge of how fluorine interacts with biological systems.

This special issue of *Journal of Fluorine Chemistry* brings together a series of papers that focuses on several important aspects of fluorine in medicinal chemistry, including synthesis, mechanistic studies, biological consequences of fluorine incorporation, and biomedicinal applications. In the first of two reviews, the application of fluorinated molecules in the development of enzyme inhibitors is reviewed. A second review covers the important area of fluorinated nucleosides. Related to this, three research reports deal with preparation of fluorinated aza-nucleoside, fluorinated thio-nucleosides and new fluorinated uracil derivatives, respectively. Three papers exemplify different approaches to fluorinated amino acids (histidine, oxindol-2-alanine, and proline), including enantioselective syntheses, while the effect of fluorine on stereocontrol in the synthesis of fluorinated peptidomimetics is described in another contribution. Effects of fluorine substitution on biological activity are illustrated in reports on the development of new fluorinated taxoids as anticancer agents and fluorinated cyclopropylamines as copper amine oxidase inhibitors. A contribution describing a fluorine scan investigates fluorophobic and fluorophilic interactions between the carbon–fluorine bond and enzyme active site residues, providing further insight into the interactions of fluorinated small molecules with macromolecular recognition sites. Synthetic methods that are reported include a paper dealing with the developing field of fluorinations in super acids. In addition, papers describing fluorination of steroids with elemental fluorine, copper catalyzed construction of fluorinated heterocyclic rings using fluorinated building blocks, and a continuous flow reductive amination route to fluorinated carbonyl compounds are included. The application of F-18 in PET scanning is illustrated through the labeling of a human epidermal growth factor antibody with an F-18-labeled small molecule to develop a prognostic tool for breast cancer. Together these contributions provide a well-rounded sampling of current research in the important field of fluorine in medicinal chemistry.

As guest editor, I am grateful to the diligent efforts of all of the authors in providing these manuscripts that together provide an excellent perspective of this exciting and important field.

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