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Laboratory profile

Profile of the "Green Organic and Medicinal Chemistry" research group at the University of Massachusetts Boston

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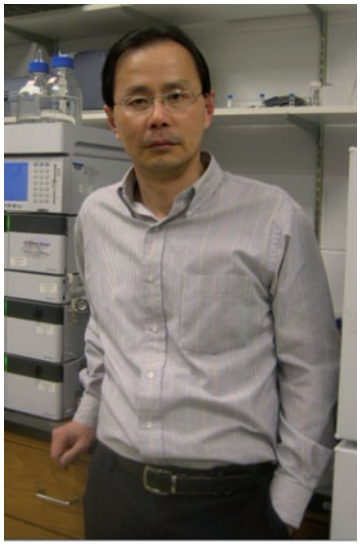
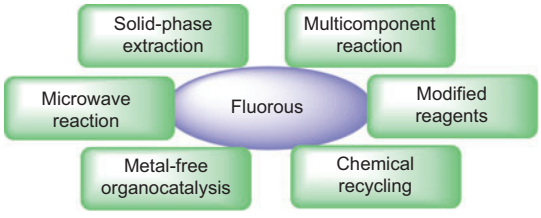


The group

The research group of Dr. Wei Zhang at the Department of Chemistry, University of Massachusetts Boston is focused on implementation of the twelve principles of green chemistry to organic synthesis and medicinal chemistry [1]. Over the years, Wei Zhang's group has developed a streamlined fluorous technology platform and demonstrated its efficiency and feasibility in high-throughput synthesis and parallel synthesis of compound libraries for lead generation and optimization [2, 3]. Fluorous technology has many green chemistry aspects, such as chromatography-free separation, energy-focused microwave reactions, atom economic multicomponent reactions, chemical recycling and toxic metal-free organocatalysis (Scheme 1) [4]. Wei Zhang's group has established a number of academic and industry collaborations for the development of new fluorous techniques for drug discovery and green chemistry applications.

The team leader

Wei Zhang received his PhD degree in chemistry from the University of Pittsburgh under the supervision of the late Prof. Paul Dowd. His PhD thesis was on the topic of development of new free radical ring-expansion and annulation reactions [5]. After a 2-year research assistant professor appointment at the same university, he joined DuPont Agricultural Chemicals and worked on the discovery of new herbicides and insecticides. In 2001, Wei Zhang returned to Pittsburgh to become one of the founding members of Fluorous Technologies, Inc. and was later promoted to director of Discovery Chemistry. He started his current position at the University of Massachusetts Boston as an associate professor in 2008. He is the director for the Center for Green Chemistry and leads the effort in the program of PhD in Green Chemistry. He is currently an editor of *Green Processing and Synthesis* (De Gruyter), associate editor of *Molecular Diversity* (Springer), and an advisory board member of *ACS Combinatorial Science*. He serves on the advisory boards of Green Chemistry Commitment and the ACS Green Chemistry Institute Curriculum Committee. Over the years, he has published 136 peer-reviewed papers. A book coedited with Dr. Berkeley Cue entitled *Green Techniques for Organic and Medicinal Applications* will be published by Wiley in the summer of 2012.

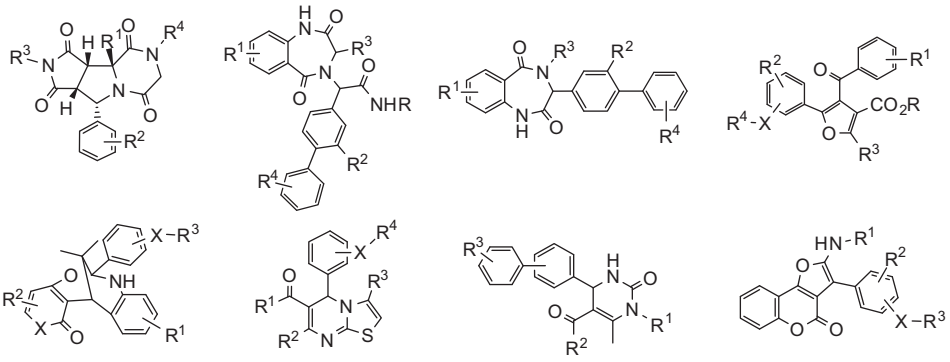


Scheme 1 Green aspects of fluorous chemistry.

Current research activities

Diversity-oriented synthesis (DOS)

The research effort on this topic has been focused on the development of fluorous linker-assisted DOS of drug-like molecules [6]. The efficiency and green chemistry advantages of fluorous technology have been demonstrated in the preparation of compound libraries for biological screenings. Some recent library scaffolds are shown in Scheme 2.



Scheme 2 Selected library scaffolds prepared by fluorous synthesis.

Fluorous diasteoremeric mixture synthesis (FDMS)

Wei Zhang's group recently introduced FDMS as a new technique to increase the efficiency of making biologically interesting diastereomers. Diastereomers bearing the same fluorous linker could be collected in the same fraction by fluorous solid-phase extraction (F-SPE). The fluorous mixture can be treated as a single component in the multistep synthesis. After the cleavage of the fluorous tag, the final products were separated by preparative liquid chromatography to provide individual diastereomers. In FDMS of hydantoin-fused hexahydrochromeno[4,3-*b*]pyrrole, eight diastereomers of the final products were produced, and six of them were successfully isolated (Scheme 3) [7]. This technology has great potential in the synthesis of diasteoreomers for quantitative structure activity relationship (QSAR) study in drug discovery.

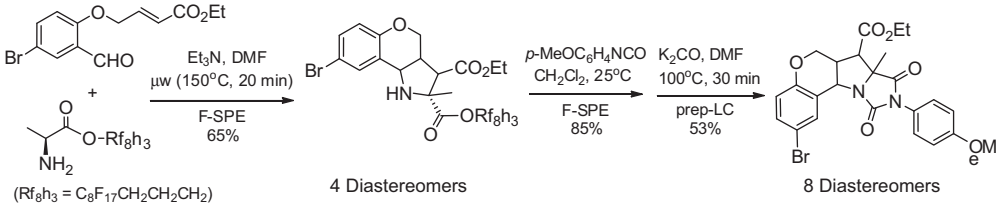
Recycable Fluorous Organocatalysis

Metal-free organocatalysis is an important topic in green chemistry. However, high catalyst loading and difficult catalyst recovery are two major challenges that need to be addressed. The Wei Zhang group introduced several fluorous organocatalysts to solve the separation issues. These catalysts include imidazolidinone (MacMillan catalyst) for asymmetric Diels-Alder reactions, pyrrolidine-thiourea for α-chlorination of aldehydes and DHQD-thiourea for fluorination (Scheme 4) [8]. In all cases, fluorous catalysts have excellent reactivity, selectivity and recyclability.

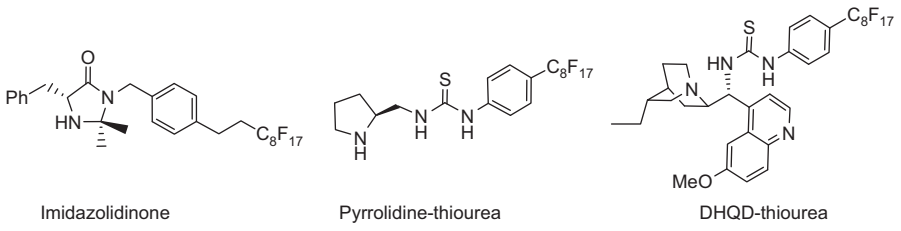
Other than the fluorous and green chemistry projects described above, Wei Zhang has collaborations with the Dana-Farber/Harvard Cancer Center and the Howard Hughes Medical Institute on medicinal chemistry and biological projects. He also collaborates with Prof. Jianpin Zou at Suzhou University on synthetic free radical chemistry [9].

The University

University of Massachusetts Boston is the only public research university in the greater Boston area. It has a



Scheme 3 Fluorous diasteoremeric mixture synthesis.



Scheme 4 Fluorous organocatalysts for enantioselective reactions.

strong tradition in green chemistry and a long list of alumni who are pioneers and leaders in this area, such as Dr. John Warner (President of the Warner-Babcock Institute for Green Chemistry), Prof. Paul Anastas (Former US EPA Assistant Administrator, Professor at Yale University), Dr. Berkeley Cue (Chair of the American Chemical Society's Green Chemistry Institute Governing Board) and Dr. Amy Cannon (Executive Director at Beyond Benign). The Chemistry Department established the first doctoral program in Green Chemistry approximately 10 years ago. Fourteen graduate students have been awarded the PhD in Chemistry/Green Chemistry. The department was involved in the organization of the Third International Symposium on Green Processing in the Pharmaceutical & Fine Chemical Industries, has established a green chemistry exchange program with Nanjing University of Science and Technology and has offered the Green Chemistry summer workshop to undergraduate students from Kyung Hee University (South Korea). All these activities indicate the national and international standing of the green chemistry program at the University of Massachusetts Boston.

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