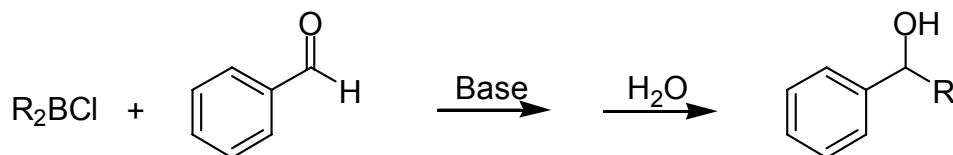


A. SYNTHETIC/MEDICINAL CHEMISTRY

One of the primary goals of my research is the development of new synthetic methods. Organoboranes are frequently, but not exclusively, employed in our studies due to the fact that they can be prepared containing a wide variety of functional groups; they are unique, reactive intermediates. Current research efforts are focused on the addition of borane reagents to carbonyl compounds. These studies center on the stereochemical consequences of the additions as well as the potential use of chiral boron reagents to generate stereodefined products.



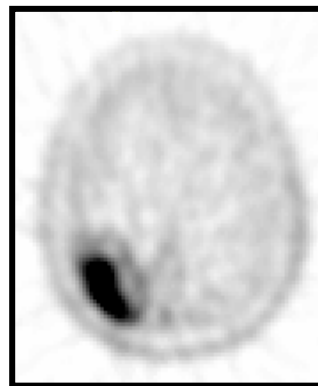
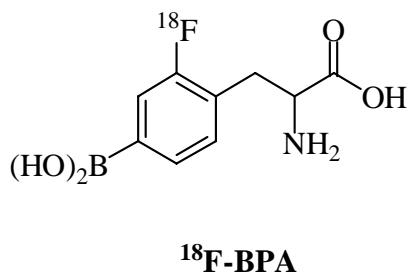
Other investigations involve the use of boron reagents in new oxidation and reduction sequences. These studies utilize a variety of new synthetic methodologies. Organometallic reagents based on tin, aluminum and zirconium are also used in our research program.

My students and I are actively involved in the development of new methods for synthesizing a physiologically active reagents. Current research targets include drugs which localize in lung and brain tumors. These agents often contain boron so that the tumor can be treated by boron neutron capture therapy.

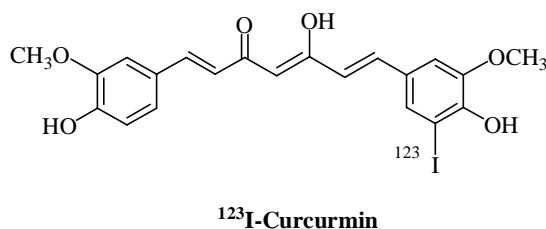
B. RADIOPHARMACEUTICAL

The objective of this project is to develop organic syntheses of physiologically active agents containing carbon, halogen, and nitrogen isotopes. These materials are used in diagnostic nuclear medicine studies at the Medical and Health Sciences Division of Oak Ridge National Laboratory and the Radiology Department of the U.T. Hospital. One of the recent trends in nuclear medicine has been the use of short lived positron emitters such as ^{18}F (110 min. half life) as medical tracers. My research group has been active in the area of rapid

syntheses via organometallic reactions; we have begun to utilize our expertise for the incorporation of radioisotopes. Current projects involve the rapid synthesis of a fluorine-18 labeled amino acid for identifying brain tumors using positron emission tomography. The image on the right was generated using ^{18}F -labeled *para*-boronophenylalanine (BPA).



Additional projects involve the development of new halogenation reactions using polymeric and solid state precursors. These reactions will be used to synthesize potential brain, heart and lung imaging agents. The students involved in these projects develop the syntheses and then have the opportunity to follow the projects through the pre-clinical studies. One of our current projects is focused on the detection of amyloid deposits *in vivo*. An example of an animal study involving the injection of a radioiodinated curcumin-based drug in a live mouse with intestinal amyloid deposits is presented in the figure on the next page (the red color denotes the location of the drug.) Other molecules under investigation are targeted to lung tumors, sleep disorders, and breast cancer.



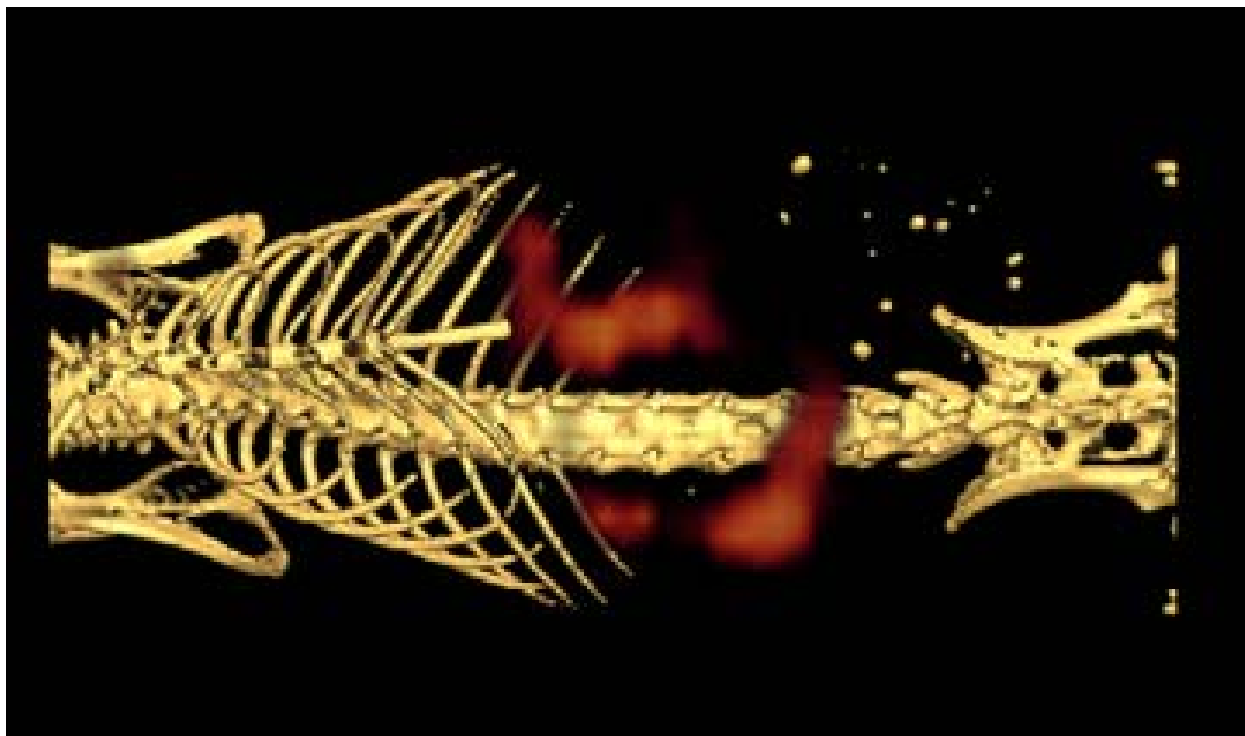
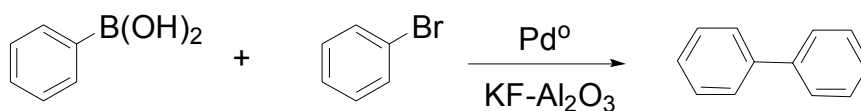


Figure 1. Radioimaging of amyloid in a Balb/C mouse. Image is a co-registered SPET/CT image of a mouse injected with the iodine-123 labeled curcumin. Amyloid is clearly visible (red)..

C. ORGANIC REACTIONS ON SOLID-STATE/POLYMERS

We have discovered that alumina, silica gel and zeolite can be used to modify a number of organic reactions (deuteration, halogenation, etc.). The object of this project is to: (1) make the reactions more efficient and practical, (2) learn how reactions occur on a surface, and, (3) examine the regio- and stereochemistry of bimolecular reactions occurring on surfaces. For example, we recently developed a solid-state Suzuki coupling reaction that is more efficient than the corresponding reaction run in solution.



All students have "hands-on" experiences with the multinuclear NMR, HPLC and GLC.

D. OVERVIEW

For an overview of our current research efforts, please review the following:

- 1 Kabalka, G. W.; Yao, M.-L.; Borella, S.; Wu, Z.; Ju, Y.-H.; Quick, T. "Boron Trihalide Mediated Alkyne-Aldehyde Coupling Reactions: A Mechanistic Investigation." *J. Org. Chem.*, **2008**, *73*, 2668-2673.
- 2 Yao, M.-L.; Borella, S.; Quick, T.; Kabalka, G. W. "Boron Trihalide Mediated Haloallylation of Aryl Aldehydes: Reaction and Mechanistic Insight." *Dalton Trans.*, **2008**, 776-778.
- 3 Kabalka, G. W.; Borella, S.; M.-L. Yao. "Boron Trihalide Mediated Substitution of Hydroxyl Groups with Alkenyl, Alkynyl, and Allyl Moeties." *Synthesis*, **2008**, 325-329.
- 4 Tang, G.; Zheng, W.; Yu, M; Kabalka, G. W.; "A Facile Synthesis of *N*-Succinimidyl 4-[¹⁸F]fluorobenzoate (¹⁸F]SFB) for Protein Labeling." *J. Labelled Compds. Radiopharm*, **2008**, *51*, 68-71
- 5 Kabalka, G. W.; Naravane, A.; Zhao, L.-L "Microwave Enhanced Cross-Coupling Involving Alkenyl- and Alkynyltrifluoroborates." *Tetrahedron Lett.* **2007**, *48*, 7091-7093.
- 6 Kabalka, G. W. "Isotope Incorporation via Organoboranes." *J. Labelled Compd. Radiopharm.*, **2007**, *50*, 888-894.
- 7 Kabalka, George W.; Yao, Min-Liang; Borella, Scott; Goins, Laura K. "Iron Trichloride Mediated Allylation of Lithium Alkoxides through an Unusual Carbon-Oxygen Bond Cleavage." *Organometal.* **2007**, *26*, 4112-4114.
- 8 Kabalka, George W.; Yao, Min-Liang; Borella, Scott. "Generation of Cations from Alkoxides: Allylation of Propargyl Alcohols." *J. Am. Chem. Soc.* **2006**, *128*, 11320-11321.
- 9 Kabalka, G. W.; Bollu, V.; Chen, C. "Baylis-Hillman Chemistry: Synthesis of Cis- and Trans- α -Methylene- γ -Lactones," *Tetrahedron Lett.* **2006**, *47*, 4187-4189.
- 10 Kabalka, G. W.; Yao, M.-L. "The Synthesis and Use of Boronated Amino Acids for Boron Neutron Capture Therapy," *Anti-Cancer Agents in Medicinal Chemistry* **2006**, *6*, 111-125.