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Departments of Chemistry,
Medicinal and Biological Chemistry

Frontiers in Chemistry
Lecture Series

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Development of Proof-of-Concept Chemical Probes Targeting Novel Biological Targets

Professor William R. Roush
Scripps Research Institute, Florida

4:00 p.m. Friday, October 4th, 2013
WO 1201

William R. Roush

Professor and Executive Director of Medicinal Chemistry and Associate Dean of Scripps' Kellogg Graduate School in Jupiter. Florida

Dr. William R. Roush, a native of Chula Vista, CA, received the Bachelors Degree in Chemistry, Summa Cum Laude, from the University of California at Los Angeles in 1974, where he performed undergraduate research with Professor Julius Rebek, and the Ph. D. Degree in Chemistry from Harvard University in 1977 under the direction of Professor R. B. Woodward. After an additional year as a postdoctoral associate in Woodward's laboratory, he joined the Massachusetts Institute of Technology as Assistant Professor. He moved to Indiana University in 1987, and was promoted to the rank of Professor in 1989 and Distinguished Professor in 1995. In 1997 he moved to the University of Michigan as the Warner Lambert/Parke Davis Professor of Chemistry. He served as Chair of the Department of Chemistry, University of Michigan, from 2002-2004. He moved to the new Scripps Research Institute in Jupiter, Florida, as Professor of Chemistry, Executive Director of Medicinal Chemistry, and Associate Dean of Scripps' Kellogg Graduate School in 2005.

Dr. Roush has been a Fellow of the Alfred P. Sloan Foundation, an Eli Lilly Grantee, and the holder of the Roger and Georges Firmenich Career Development Chair in Natural Products Chemistry at MIT. He received a Merck Faculty Development Award in 1981, the 1992 Alan R. Day Award of the Philadelphia Organic Chemist's Club, the 1994 Arthur C. Cope Scholar Award of the American Chemical Society, and the 1996 American Chemical Society Akron Section Award. In 1998 he received a Merit Award from the National Institute of General Medical Sciences, and in 1999 he received a Distinguished Faculty Achievement Award from the University of Michigan. In 2002 Dr. Roush received the Paul G. Gassman Distinguished Service Award of the American Chemical Society Division of Organic Chemistry, and in 2004 he received the American Chemical Society Ernest Guenther Award in the Chemistry of Natural Products. In 2006, Dr. Roush was elected Fellow of the American Association for the Advancement of Science. Most recently, in 2009 Dr. Roush was elected to the inaugural class of Fellows of the American Chemical Society.

Dr. Roush has served terms as Secretary-Treasurer and Chairman of the ACS Division of Organic Chemistry, and as Chairman of the NIH Medicinal Chemistry Study Section. He currently is Associate Editor of the *Journal of the American Chemical Society*, and serves on the Editorial Advisory Board of *Organic Letters*. He is a Director of *Organic Reactions, Inc.,* and of *Organic Syntheses, Inc.,* and is a consultant for several companies.

Dr. Roush's research interests focus on the stereocontrolled synthesis of stereochemically complex natural products, and on the design and development of new reactions and synthetic methods. He is known for his stereochemical studies and synthetic applications of the intramolecular Diels- Alder reaction and his work in the area of asymmetric and acyclic diastereoselective synthesis, specifically the use of tartrate ester modified allylboronates and other allylmetal compounds for the aldol-like construction of propionate-derived systems. He has also made important contributions the synthesis of deoxyglycosides and polyhydroxylated natural products (his total synthesis of olivomycin A is particularly noteworthy), and to the design and synthesis of inhibitors of cysteine proteases targeting important human pathogens (e.g., *Trypanosoma*, *Plasmodium* and *Entamoeba* species). Since moving to Scripps Florida, his program in chemical biology and medicinal chemistry has expanded to include research on the development of inhibitors of kinases, inhibitors and activators of nuclear receptors, and small molecule inhibitors of carboxylic acid transporters as potential therapeutic agents.

Selected Publications

Articles

1. W. R. Roush, H. R. Gillis, and A. I. Ko, "Stereochemical Aspects of the Intramolecular Diels-Alder Reactions of Methyl Deca-2,7,9-trienoates. 3. Thermal, Lewis-Acid Catalyzed, and Asymmetric Cyclizations," *J. Am. Chem. Soc.* **1982**, *104*, 2269.
2. W. R. Roush, S. L. Gwaltney, III, J. Cheng, K. A. Scheidt, J. H. McKerrow, and E. Hansell, "Vinylsulfonates and Vinylsulfonamides: Potent, Irreversible Inhibitors of Cysteine Proteases," *J. Am. Chem. Soc*., **1998**, *120*, 10994.
3. W. R. Roush, R. A. Hartz and D. J. Gustin, "Total Synthesis of Olivomycin A", *J. Am. Chem*. *Soc*., **1999**, *121*, 1990.

4. W. R. Roush and C. E. Bennett, "A Highly Stereoselective Synthesis of 2-Deoxy-β-Glycosides using 2-Deoxy-2-Iodo-Glucopyranosyl Acetate Donors", *J. Am. Chem. Soc*., **1999**, *121*, 3541.
5. E. Flamme and W. R. Roush, "Enantioselective Synthesis of 1,5-Anti and 1,5-Syn Diols Using a Highly Diastereoselective One-Pot Double Allylboration Reaction Sequence," *J. Am. Chem. Soc.*, **2002**, *124*, 13664.
6. L. A. Solt, N. Kumar, P. Nuhant, Y. Wang, J. L. Lauer, J. Liu, M. Istrate, T. M. Kamenecka, W. R. Roush, D. Vidovic, S. C. Schürer, J. Xu, G. Wagoner, P. D. Drew, P. R. Griffin, and T. P. Burris, "Suppression of T_H17 Differentiation and Suppression of Autoimmunity by a Selective Synthetic ROR Ligand," *Nature* **2011**, *472*, 491.
7. M. Chen and W. R. Roush, "Enantioconvergent Hydroboration of a Racemic Allene: Enantioselective Synthesis of (*E*)-δ-Stannyl-*anti*-Homoallylic Alcohols via Aldehyde Crotylboration," *J. Am. Chem. Soc*. **2011**, *133*, 5744.
8. M. Chen and W. R. Roush, "Highly Stereoselective Synthesis of Anti, Anti-Steriotriads: A Solution to the Long-Standing Problem of Challenging Mismatched Double Asymmetric Crotylboration Reactions," *J. Am. Chem. Soc*., **2012**, *134*, 3925.
9. P. Nuhant and W. R. Roush, "Enantio- and Diastereoselective Synthesis of N-Acetyl Dihydrotetrafibricin Methyl Ester," *J. Am. Chem. Soc*. **2013**, *135*, 5340.
10. P. Nuhant, C. Allais and W. R. Roush, "(Diisopinocampheyl)borane-Mediated Reductive Aldol Reactions: Highly Enantio- and Diastereoselective Synthesis of Syn-Aldols from N-Acryloylmorpholine," *Angew. Chem. Int. Ed*. **2013**, *52*, 8703.

Frontiers in Chemistry Lecture Series

The Department of Chemistry's Frontier's in Chemistry Lectureship Series was inaugurated in 1984 with a lecture by George S. Hammond. The series has remained active with lectures each year since, including chemistry Nobelists H. C. Brown, R. H. Grubbs, E. Negishi, and H. A. Hauptman. The "Frontiers" lecturers have also included Al Cotton, Alan Fersht, Tom Kaiser, Sid Hecht, Ron Breslow, Ken Houk, JoAnne Stubbe, Mike Marletta, John Arnold and Steve Benkovic. The lecture series is sustained by an endowed fund that was initiated by donations from University of Toledo chemistry faculty members dating back to 1981.