Robert E. Maleczka, Jr.

Synthetic Organic Chemistry

Professor

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B.S., 1984,
Univ. of Illinois at Urbana-Champaign;

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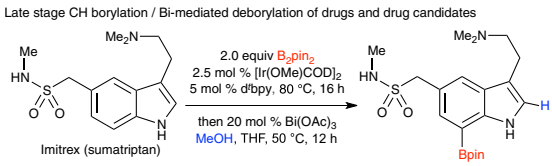
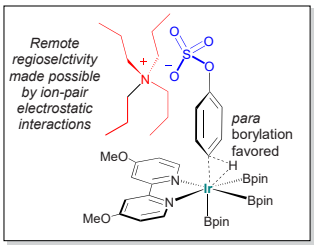
Our group is interested in a) green chemistry, b) the invention of new reactions and strategies in organic synthesis, and c) target synthesis of molecules with interesting properties ranging from biologically important natural products to nanomaterials.

Green Chemistry: Central to our research is the development of efficient and environmentally benign reactions and strategies. The Pharmaceutical Roundtable of the American Chemical Society's Green Chemistry Institute deemed cross-couplings that avoid haloaromatics as their top aspirational reaction. In collaboration with Professor Mitch Smith, we are inventing such reactions. Specifically, we are using **catalytic C–H activation/borylation**, often combined with subsequent chemical events, to generate pharmaceutically relevant

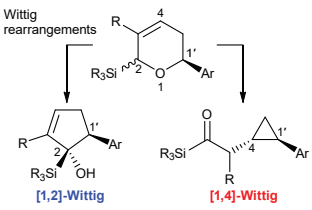


building blocks for organic synthesis and the late stage functionalization of drugs and drug candidates.

Invention of New Reactions: The principles of green chemistry also motivate us to create new synthetic methods. Within our catalytic borylation program, an example is our recently disclosed use of ion-pairing, where the alkyl groups of the cation create a steric shield that facilitates previously unheard of levels of para selectivity.



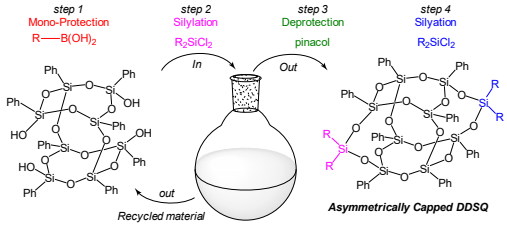
We are also focusing on the employment of organosilanes as both reagents and substrates in chemical transformations ranging from **Wittig rearrangements** to new approaches to double-decker silsesquioxanes (DDSQ's) for materials applications.



Since their discovery more than 70 years ago, Wittig rearrangements have evolved into powerful tools for the isomerization of α-metalated ethers into alkoxides. Relative to the [2,3]- and [1,2]-shifts, [1,4]-Wittig rearrangements are unique in their ability to generate stereodefined enolates. In addition, [1,4]-Wittig rearrangements have the potential to transfer chirality and stereoselectively form adjacent chiral centers. As such, we continue to study these mechanistically fascinating and synthetically intriguing rearrangements.

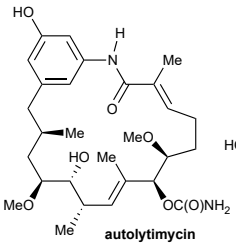
We have also teamed up with Chemical Engineering and Materials Science Professor Andre Lee, to apply our synthetic expertise to another remarkable class of compounds, namely **silsesquioxanes**. These caged structures have garnered significant attention over their ability to meet the demands of medical, aerospace and materials industries. This is due to the well-defined spatial dimensions, the presence of seven inert peripheral organic moieties to accommodate solubility and processability, and one polymerizable reactive organic group.

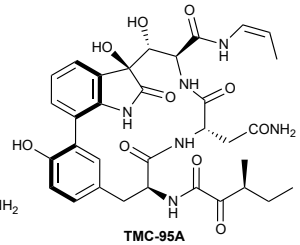
Like our other projects, we approach the synthesis of silsesquioxane through the lens of green chemistry. An example of this can be seen in our development of the first direct synthetic route leading to asymmetrically functionalized DDSQ compounds. By way of our route over 50% of the starting DDSQ tetraol that could have



otherwise contributed toward the synthesis of unwanted side products is recovered with a high purity and can be used in another cycle of synthesis. Efforts to use these compounds as nano-linkers to two different block copolymers are underway in our lab.

Target Synthesis: A unifying thesis behind all of our methodological and mechanistic studies is that the chemistry to emerge from such studies should be **applicable to real synthetic problems**. We view target synthesis as the best proof of this concept. For example, as part of our green chemistry program, we look to make TMC-95A and autolytimycin by the strategic application of our own synthetic methods.





Selected Publications

"Balancing Reactivity, Regioselectivity and Product Stability in Ir-catalyzed Ortho C–H Borylations of Anilines by Modulating the Diboron Partner" Montero Bastidas, J. R.; Yadav, A.; Lee, S.; Ghaffari, B.; Smith, M. R., III; Maleczka, R. E., Jr. *Org. Lett.* **2024**, 26, 5420–5424.

"On the Inconsistencies in Previously Reported Protections of the Catechol Moiety of L-DOPA" Yang, C.; Fan, J.; Maleczka, R. E., Jr. *Tetrahedron. Lett.* **2024**, 144, 155150.

"Iridium-Catalyzed Anti-Markovnikov Hydrosilylation of Vinylbenzenes with a Bis-Silane-Capped Double-Decker Silsesquioxane" Walsh, S. P.; Lee, A.; Maleczka, R. E., Jr. *Organometallics* **2024**, 43, 1085–1094.

"Simple and Green Preparation of Tetraalkoxydiborons and Diboron Diolates from Tetrahydroxydiboron" Fornwald, R. M.; Yadav, A.; Montero Bastidas, J. R.; Smith, M. R., III; Maleczka, R. E., Jr. J. *Org. Chem.* **2024**, 89, 6048–6052.

"Access to C(sp3) Borylated and Silylated Cyclic Molecules: Hydrogenation of Corresponding Arenes and Heteroarenes" Chhabra, A.; Reich, S.; Shannon, T. M.; Ghaffari, B.; Maleczka, R. E., Jr.; Smith, M. R., III *RSC Advances* **2024**, 14, 10590–10607.

"Regiochemical Switching in Ir-Catalyzed C–H Borylation by Altering Ligand Loadings of N,B-Type Diboron Species" O'Connell, A. C.; Mansour, P. A.; Maleczka, R. E., Jr.; Smith, M. R., III *Org. Lett.* **2023,** 25, 8057–8061.

"Steric Shielding Effects Induced by Intramolecular C–H•••O Hydrogen Bonding: Remote Borylation Directed by Bpin groups" Montero Bastidas, J. R.; Chhabra, A.; Feng, Y.; Oleskey, T. J.; Smith, M. R., III; Maleczka, R. E.; Jr. *ACS Catal.* **2022**, 12, 2694–2705.