Inorganic Seminar on October 31, 2012
Room 1315 at 3:30 PM

No More Nucleophiles: Direct, Selective Cross Coupling of Electrophiles

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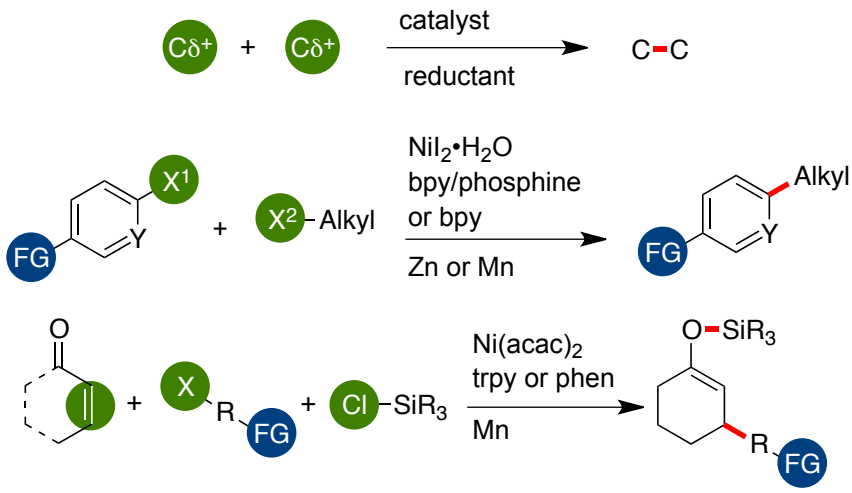

Abstract. The catalytic coupling of nucleophilic carbon reagents with carbon electrophiles has become a cornerstone of modern synthesis. The built-in bias of these substrates enables selective cross-coupling, but the need for pre-formed organometallic reagents (1) limits the number of commercially available derivatives; (2) incurs extra steps for their synthesis that are often temperature, air, and moisture sensitive; and (3) reduces the number of accessible target molecules due to functional-group compatibility and stability problems. These limitations, in turn, influence which potential drugs are synthesized and tested. Instead of synthesizing the best molecules, we often must settle for what can be easily made. Substitution of a second electrophile for the organometallic partner in cross-couplings offers the potential to dramatically increase the number and types of molecules that can be easily made because of the large number of commercially available carbon electrophiles (>1 million R-X vs. ~5 thousand R-B(OH)2) and the low cost of all components.

While the selective union of two different electrophiles introduces its own challenges, such as selectivity for cross-coupling over dimerization and the generally limited understanding of the mechanisms, we have recently validated this approach. Reductive analogs to conventional cross-coupling, conjugate addition/enolate trapping, and ketone synthesis will be discussed, with a particular emphasis on our current understanding of the mechanistic origin of the observed cross-selectivity.

Biosketch. Daniel graduated from Columbia University in 2000, where he conducted research on helicenes with Thomas Katz. During his PhD work with Jonathan Ellman at the University of California (2000-2005), Daniel worked on improved methods for the synthesis and use of *tert*-butanesulfinamide. Following postdoctoral work on Ir-catalyzed allylation chemistry with John Hartwig, Daniel began his independent career at the University of Rochester in 2008. Daniel has been the recipient of an NSF pre-doctoral fellowship, an NIH postdoctoral fellowship, and several teaching awards. His research program is currently supported by the NIH.