## Organic Chemistry Hirschmann Lecture Series

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## On the Invention of New Synthetic Methods and Their Impact On Synthetic Strategy to Bioactive Targets

The improvement of synthetic efficiency requires that the fundamental tools of synthesis, the reactions themselves, become more efficient-i.e. more selective and more atom economic. The ideal reaction from the point of view of stoichiometry is an addition wherein 100% of the mass of all starting materials converts into mass of the product (assuming a quantitative yield) and anything else is needed only catalytically. Unfortunately, most synthetically important reactions are not additions although several are such as the Diels-Alder and aldol reactions. Increasing the repertoire of addition reactions will be outlined. Special attention will focus on the utility of such new methodology in evolving more efficient synthetic strategies to complex bioactive natural products.

The chemistry focuses on ruthenium catalyzed processes. Maintaining the same oxidation level streamlines synthetic strategy as well as be more atom economic. Redox isomerization is one approach to accomplish this task and leads to new syntheses of oxygen and nitrogen heterocycles. The alkene-alkyne coupling has proven to be very effective both inter- and intramolecularly. While ruthenium remains the major catalysts, complexes of other metals also lead to interesting and unprecedented reactivity for atom economy. Among them, palladium complexes have proven to be quite interesting. Using atom economic reactions also has led to novel strategic insights into complex targets. A strategy for the synthesis of the amphidinolide, laulimalide, and bryostatin families reveals the power of these concepts.