On Inventing Reactions for Atom Economy

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 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 bryostatin family reveals the power of these concepts.

About the Speaker

Prof. Trost began his university training at the University of Pennsylvania (BA, 1962) and obtained a Ph.D. degree in Chemistry just three years later at the Massachusetts Institute of Technology (1965). He moved to the University of Wisconsin where he was promoted to Professor of Chemistry in 1969 and subsequently became the Vilas Research Professor in 1982. He joined the faculty at Stanford as Professor of Chemistry in 1987 and became Tamaki Professor of Humanities and Sciences in 1990. In 1994, he was presented with a Docteur honoris causa of the Université Claude-Bernard (Lyon I), France, and in 1997 a Doctor Scientiarum Honoris Causa of the Technion, Haifa, Israel. He was appointed an Honorary Professor at the Shanghai Institute of Organic Chemistry in 2006. Prof. Trost's work has been characterized by a very high order of imagination, innovation and scholarship. He has ranged over the entire field of organic synthesis, particularly emphasizing extraordinarily novel methodology. Further, he has repeatedly demonstrated how his innovative methodology allows for the simplification of many complex target oriented syntheses leading to natural products of high biological activity. The long term goal and defining mission of Professor Trost's career has been toward enhancing synthetic effectiveness. More recently, his work has focused on enantioselective catalysts via the rational design of "chiral space." This work requires a detailed grasp of the mechanistic nuances of organometallic reactions. As part of this program, he designed a new class of ligands that spontaneously forms dinuclear complexes that are proving to be especially effective at asymmetric catalysis. Another continuing theme, directed to the realities of organic synthesis in fostering commercial goals, is the strategy of "atom economy." Thus, synthetic building blocks are combined to produce complex targets in high yield with a bare minimum of debris under the guidance of carefully crafted catalysts. In this way, organic synthesis can be brought to bear in process settings to reach substances of high complexity in a commercially feasible way which minimizes environmental impact. Prof. Trost's triumphs in total synthesis include complex terpenoids, steroids, alkaloids, vitamins, antibiotics, nucleosides and macrolides. His syntheses are conducted with characteristic flair and serve as learning resources in addressing the limits of the methodology which he tends to develop independently.