

SINGAPORE CATALYSIS SOCIETY LECTURE SERIES

Transition Metal-Catalysed Organometallic Reactions that Have Revolutionised Organic Synthesis

Professor Ei-ichi Negishi
Herbert C. Brown Distinguished Professor of Chemistry
Purdue University, USA

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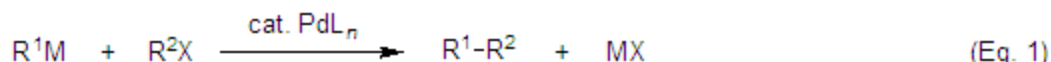
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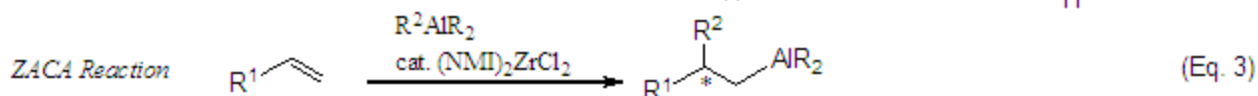
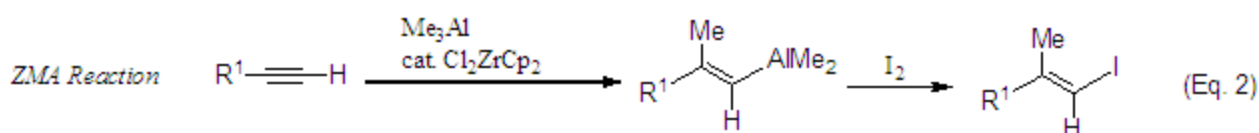
Abstract

Recognition and explorations of the only several discrete processes that transition metals can undergo for C-C (and C-X) bond formation including (1) **reductive elimination** producing coupling products, (2) **carbometalation**, (3) **migratory insertion**, and (4) **nucleophilic and electrophilic attack on ligands** have led to the discoveries and developments of a number of synthetically useful reactions.

In particular, **Pd-catalysed cross-coupling** discovered in the mid-1970's has emerged as arguably the most versatile method for C-C bond formation by coupling (Eq. 1). Significantly, it is mostly complementary with the conventional uncatalysed Grignard and organoalkali metal reactions and has thus overcome the major deficiencies associated with the latter. Indeed, the great majority of all conceivable types of cross-coupling can be efficiently and selectively carried out. (Eq. 1)



The progress in the Pd-catalysed cross-coupling has made it desirable to be able to synthesise as many conceivable types of R^1M and R^2X as possible. For the preparation of structurally most intricate and varied alkenyl and alkyl (especially chiral alkyl) reagents, hydrometalation, carbometalation, metallometalation, as well as seemingly contrathermodynamic halo- and other hetero-metalation of alkynes and alkenes have proven to be efficient, selective, and collectively versatile. Many of these processes, especially those involving carbometalation, heavily rely on transition metal catalysis, as exemplified by Zr-catalysed carboalumination of alkynes, especially methylalumination (ZMA, Eq. 2), Zr-catalysed asymmetric carboalumination of alkenes (ZACA, Eq. 3) as well as carbopalladation and acylpalladation.



Efforts towards the goal of being able to synthesise any types of alkenes through the combined use of Pd-catalysed cross-coupling and various addition reactions mentioned above are still ongoing, but the progress to date has been very fruitful.

About the Speaker



Professor Ei-ichi Negishi

Herbert C. Brown Laboratories of Chemistry

Purdue University, West Lafayette, Indiana 47907-2084, USA

E-mail: negishi@purdue.edu

Ei-ichi Negishi, H. C. Brown Distinguished Professor of Chemistry, Purdue University, grew up in Japan and received his Bachelor's degree from the University of Tokyo (1958). He then joined a chemical company, Teijin. In 1960 he came to the University of Pennsylvania on a Fulbright-Smith-Mund All-Expense Scholarship and obtained his Ph.D. degree (under Prof. A. R. Day) in 1963. He returned to Teijin but decided to pursue an academic career. In 1966, he joined Professor H. C. Brown's Laboratories at Purdue as a Postdoctoral Associate and began investigating various C—C bond forming reactions of organoboranes. He was appointed Assistant to Professor Brown in 1968. It was during the following few years that he began feeling the need for some catalytic ways of promoting organoborane reactions.

Negishi went to Syracuse University as Assistant Professor in 1972 and began his life-long investigations of *transition metal-catalysed organometallic reactions for organic synthesis*. His initial and largely unsuccessful attempts to develop a Cu-catalysed conjugate addition or substitution reaction of organoboranes soon led him to adopt a then novel strategy of considering all 60 or so non-radioactive metals as components of both stoichiometric reagents and catalysts. During the 1976-1978 period he published about 10 papers describing the Pd- or Ni-catalysed cross-coupling reactions of various organometals including those of Mg, Zn, B, Al, Sn, and Zr. Today, those involving Zn, Al, and Zr are called the *Negishi coupling*. His success in developing the Pd- or Ni-catalysed alkenylzirconiums was the beginning of many series of his subsequent investigations of organozirconium chemistry leading to the discoveries and developments of the Zr-catalysed alkyne carboalumination often called the *Negishi alkyne carboalumination* (1978-), the Zr-catalysed asymmetric alkene carboalumination (*ZACA reaction*) (1995-), and the chemistry of low-valent zirconocenes generated via Bu_2ZrCp_2 and other dialkylzirconocenes widely known as the *Negishi reagents* (1985-).

Negishi was promoted to Associate Professor at Syracuse University in 1976 and invited back to Purdue University as Full Professor in 1979. In 1999 he was appointed the inaugural H. C. Brown Distinguished Professor of Chemistry. Various awards he has received include Guggenheim Fellowship (1987), the 1996 A. R. Day Award, a 1996 Chemical Society of Japan Award, the 1998 ACS Organometallic Chemistry Award, a Humboldt Senior Researcher Award, Germany (1998 - 2001), the 2000 RSC Sir E. Frankland Prize Lectureship, and the 2007 Yamada-Koga Prize. At Purdue University, he was the recipient of the 1998 McCoy Award and the 2003 Sigma Xi Award.

Negishi has published over 400 publications including two books, one of which is *Handbook of Organopalladium Chemistry for Organic Synthesis*, 2 Vols., Negishi, E., Ed., Wiley-Interscience, New York, 2002, 3279 pp., and several patents. Collectively, these publications have been cited about 18,000 times (H-Index of 66). Negishi has been cited in Marquis Who's Who in American and Marquis Who's Who in the World. The Negishi coupling has been cited in Merck Index.