

Transition Metal Catalysts Support 21st Century Prosperity

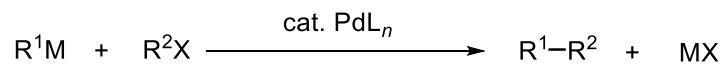
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Until recently, the majority of the 24 *d*-block transition metals, e.g., Fe, Cu, Ag, Au, etc., had been used as useful and sturdy materials. Half a century ago, a wide range of possibilities for use of *d*-block transition metals as catalysts for organic synthesis were recognized. These opportunities stem mainly from two fundamental properties of the *d*-block transition metals: (i) simultaneous presence or availability of one or more filled-nonbonding (HOMO) and empty (LUMO) valence-shell orbitals, i.e. “carbene-like,” leading to highly reactive and yet thermally stable species; and (ii) ability to undergo ready and reversible “redox” processes under one-set of reaction conditions in one vessel. These properties have led to the development of a large number of widely ranging processes including critically important C–C bond formation reactions proceeding through: (a) reductive elimination (ex. Pd-catalyzed cross-coupling), (b) carbometalation (ex. ZACA reaction), and (c) migratory insertion (ex. carbonylation including “oxo” process).

In particular, *Pd-catalyzed cross-coupling* discovered in the 1970's, especially those involving Zn, Al, Zr (1976-1978, Negishi coupling)¹ and B (1979, Suzuki coupling)², collectively have brought about "revolutionary" changes in organic synthesis. Thus, two regio- and stereodefined carbon groups of R¹M (M = Zn, Al, B, Cu, Zr, Sn, etc.) and R²X (X = I, Br, OTs, etc.) can be cross-coupled to give R¹–R² with essentially full retention of all structural features. Indeed, the Pd-catalyzed cross-coupling reactions have emerged as arguably the most widely applicable organic skeletal construction method discovered and developed over the past four decades, allowing the synthetic chemists to prepare practically all types of organic compounds. In this lecture, some of the seminal and critically important discoveries and early developments in the 1970s as well as their current scope are briefly discussed. Some of the notable discoveries and developments include (i) identification, *for the first time*, of superior properties of Pd relative to Ni as a critical element for cross-coupling,^{1b} (ii) the broad scope of Pd- or Ni-catalyzed cross-coupling with respect to metal counter-cations including Zn, Al, Zr, B, Sn, and Mg,^{1g} (iii) the

development of hydrometalation-, carbometalation-, heterometalation–Pd-catalyzed cross-coupling tandem processes for selective syntheses of alkenes, dienes, oligoenes, and oligoenynes, (iv) double metal catalysis involving Pd or Ni and added metal compounds containing Zn, In, Li, and others, and (v) realization of high turnover numbers ($\geq 10^3$ – 10^9) through the use of chelating phosphines, such as DPEphos and dppe.

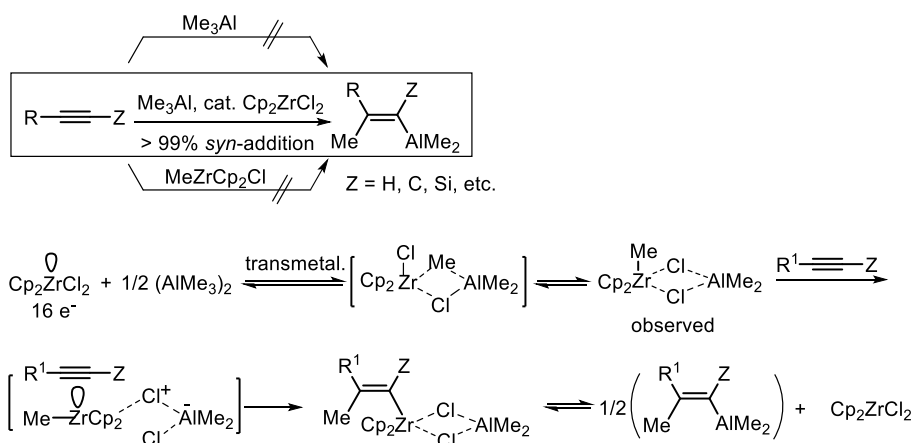


M = Zn, Al, Zr, B, Sn, Cu, etc.

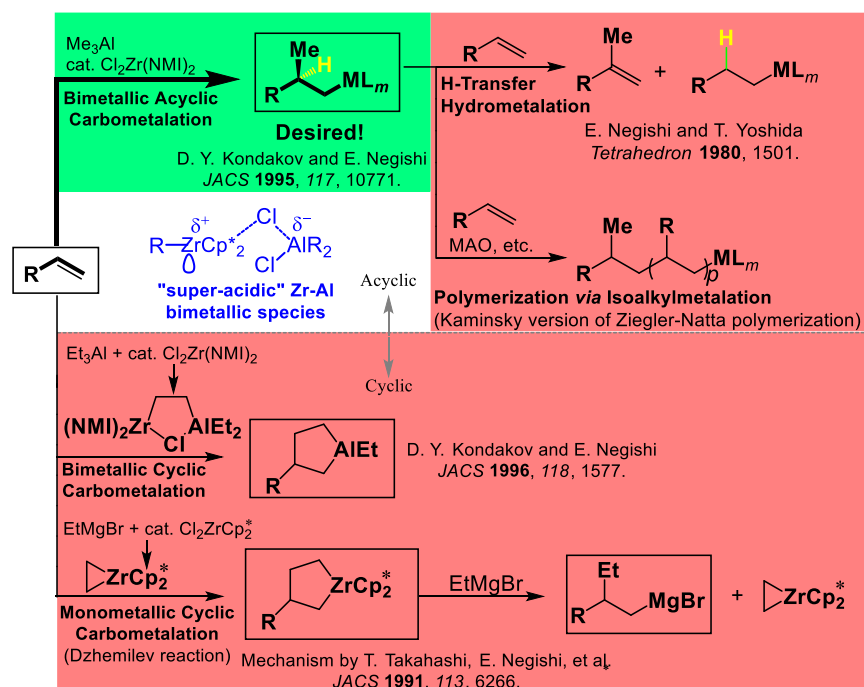
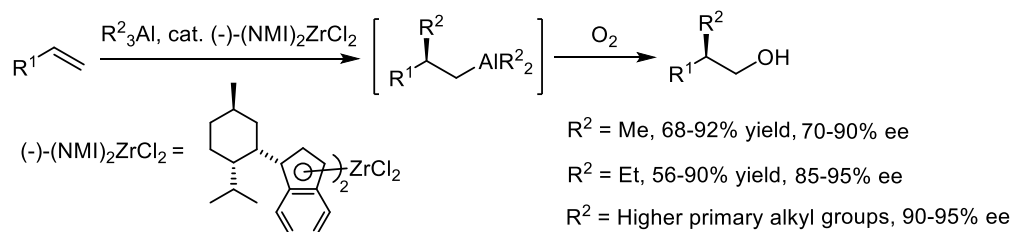
X = I, Br, OTs, etc.

Scheme 1.

The progress in the Pd-catalyzed cross-coupling has made it desirable to be able to synthesize 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 in (i) *high yields (Y)*, (ii) *efficiency (E)*, (iii) *selectivity (S)*, (iv) *economy (E)*, and (v) *safety (S)*, namely in *Y(ES)² manner*, which collectively amount to "**green and sustainable**" synthesis, hydrometalation, carbometalation, metallometalation, as well as seemingly contrathermodynamic halo- and other hetero-metalation of alkynes and alkenes have been developed and proven to be efficient, selective, and collectively satisfactory. Many of these processes, especially those involving carbometalation, heavily rely on transition metal catalysis, as exemplified by Zr-catalyzed carboalumination of alkynes, especially methylalumination (ZMA) (Scheme 2),³ Zr-catalyzed asymmetric carboalumination of alkenes (ZACA) (Scheme 3)⁴.

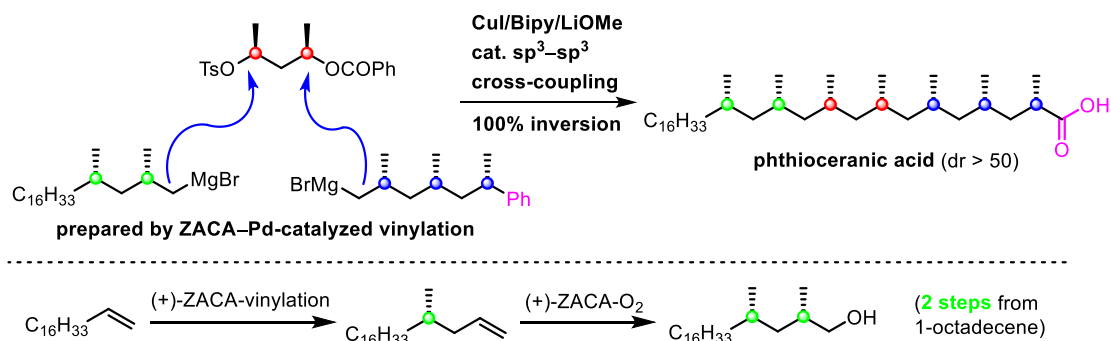


Scheme 2. Zr-catalyzed methylalumination of alkynes (ZMA).



Scheme 3. Zr-catalyzed asymmetric carboalumination of alkenes (ZACA).

The Zr-catalyzed alkyne carboalumination and the Zr-catalyzed asymmetric carboalumination of alkenes (ZACA reaction) have provided efficient and selective routes to (*E*)-trisubstituted alkenylalanes and 2-substituted chiral alkylalanes, respectively. These reactions provide two additional examples of prototypical transition metal-catalyzed organometallic reactions. Significantly, they can be readily used in combination with the Pd-, Ni- or Cu-catalyzed cross-coupling for the synthesis of trisubstituted alkenes embracing a wide variety of natural products, such as terpenoids, carotenoids, and others, as well as various chiral organics including deoxypolypropionates, saturated terpenoids, and molecules containing all-carbon quaternary stereocenters.⁵ Recently, we developed “ZACA–lipase-catalyzed acetylation–transition metal-catalyzed cross-coupling” processes for highly efficient and enantioselective syntheses of a wide range of chiral organic compounds with ultra-high enantiomeric purities.⁶



Scheme 4.

References

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