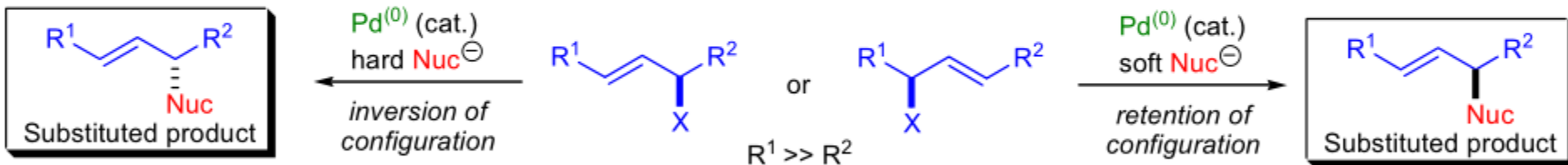
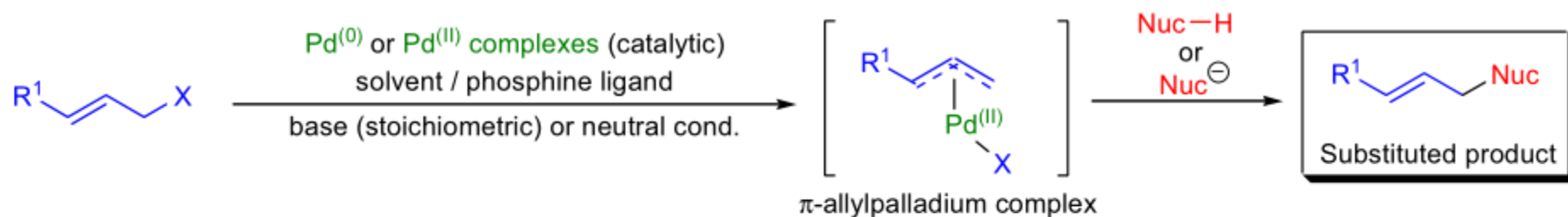


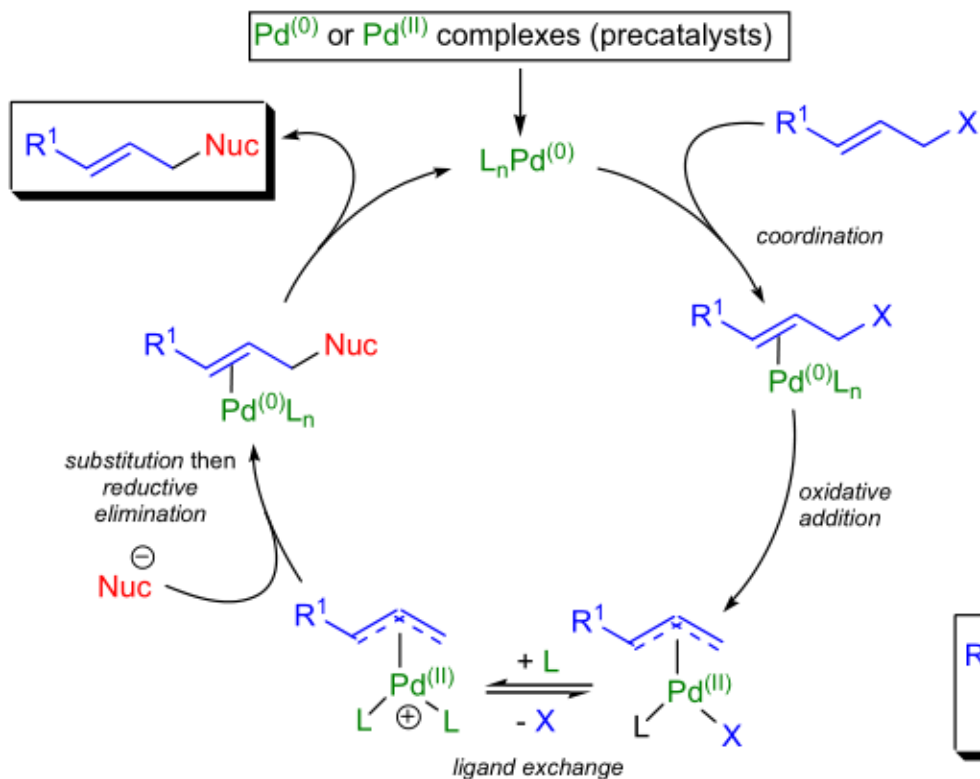
TSUJI-TROST REACTION / ALLYLATION

Electrophilic Mono- π -allylpalladium Complexes (Tsuji-Trost Reaction / Allylation)

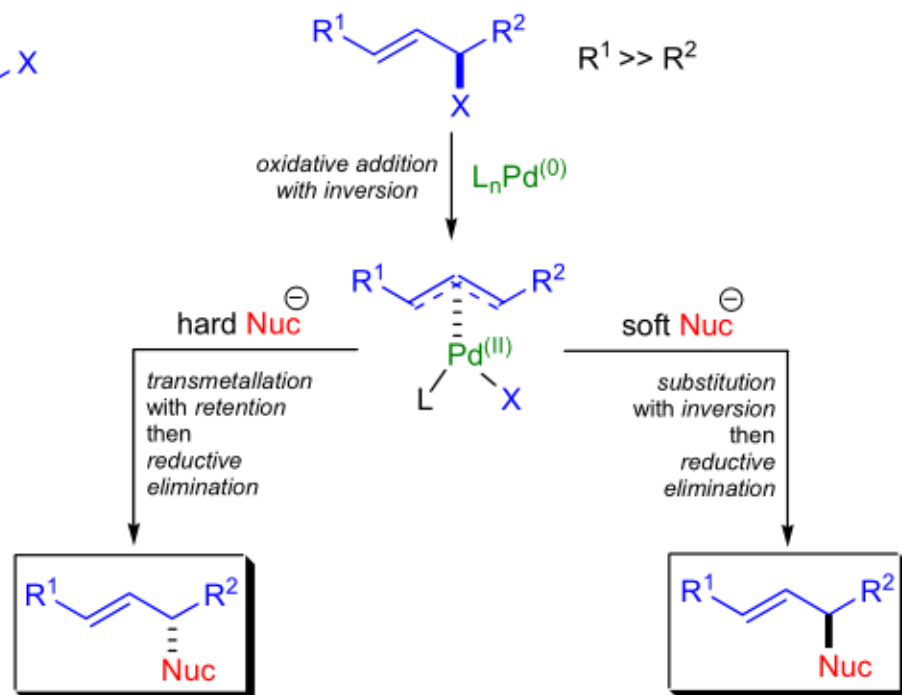


R^{1-2} = H, alkyl, aryl; X = OH, OPh, OCOR, OCONHR, OCO₂R, OP(O)(OR)₂, Cl, NO₂, SO₂Ph, NR₂, NR₃X, SR₂X
 soft Nuc-H = R³R⁴CH₂, enamines, enolates; R³⁻⁴ = CO₂R, CN, NO₂, SO₂Ph, COR, NC, N=(CMe₂), SPh, alkenyl
 Pd-complexes: Pd(PPh₃)₄, Pd₂(dba)₃, [Pd(allyl)Cl]₂; ligands: PPh₃, dba

Mechanism

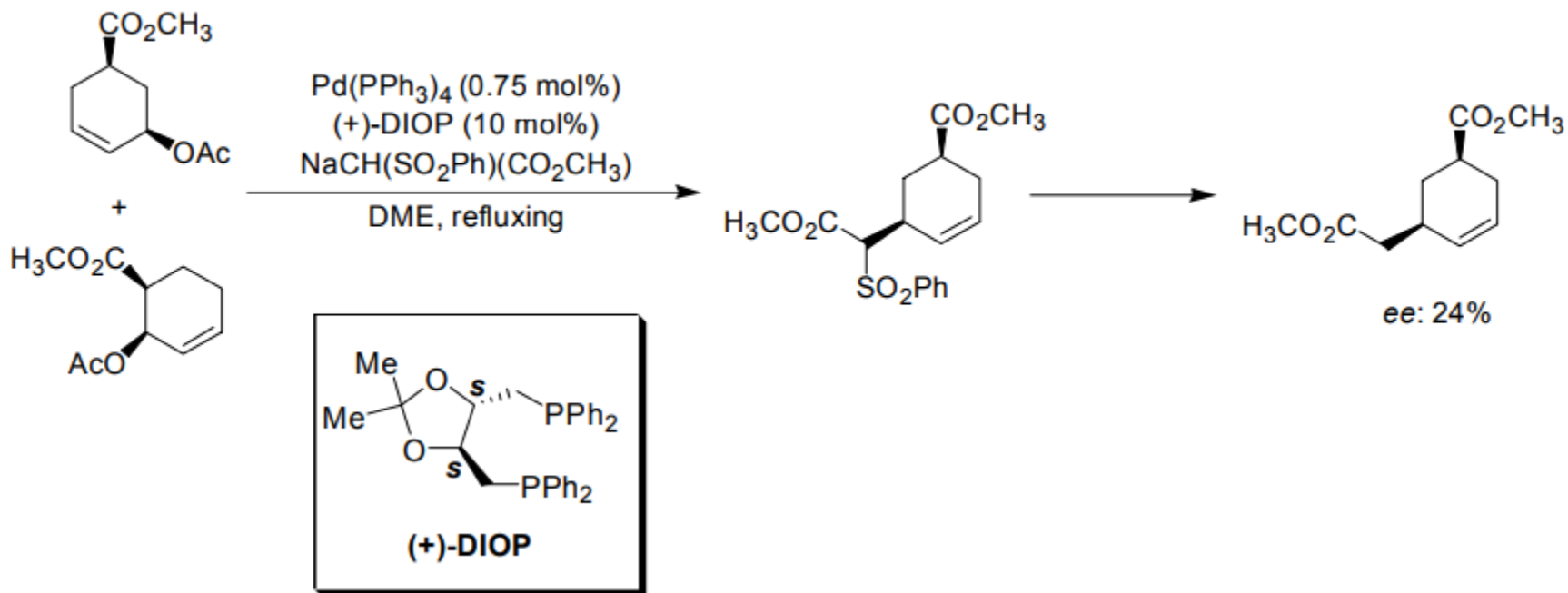


Mechanism with soft and hard nucleophiles:



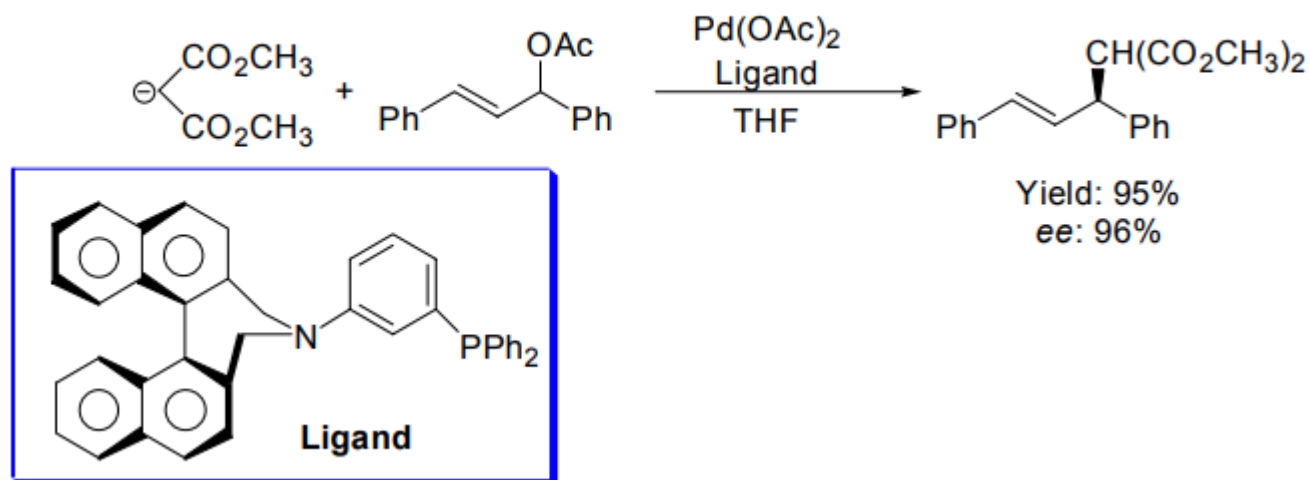
- 1) A wide range of leaving groups (X) can be utilized to form **π -allylpalladium complexes** (e.g., halides, acetates, ethers, sulfones, carbonates, carbamates, epoxides, and phosphates);
- 2) There is a marked difference in the reactivity of the various leaving groups with the following trend: $\text{Cl} > \text{OCO}_2\text{R} > \text{OAc} \gg \text{OH}$;
- 3) In the case of most substrates, the use of a stoichiometric amount of base is necessary to generate the soft nucleophiles. However, allylic carbonates undergo decarboxylation, and in the process a sufficiently basic alkoxide is formed so no extra base is needed;
- 4) The addition of the nucleophiles to the unsymmetrical π -allylpalladium complexes is regioselective and **favors the least substituted allyl terminus** regardless of the initial position of the leaving group;
- 5) Occasionally the regioselectivity can be influenced by the nature of the ligand and the nucleophile;
- 6) Optically active substrates are substituted by soft nucleophiles with an overall retention of configuration (double inversion), while hard nucleophiles give rise to products with an overall inversion of configuration (π -allylpalladium complexes are transmetallated).

First Asymmetric Catalytic Tsuji-Trost-type Reaction



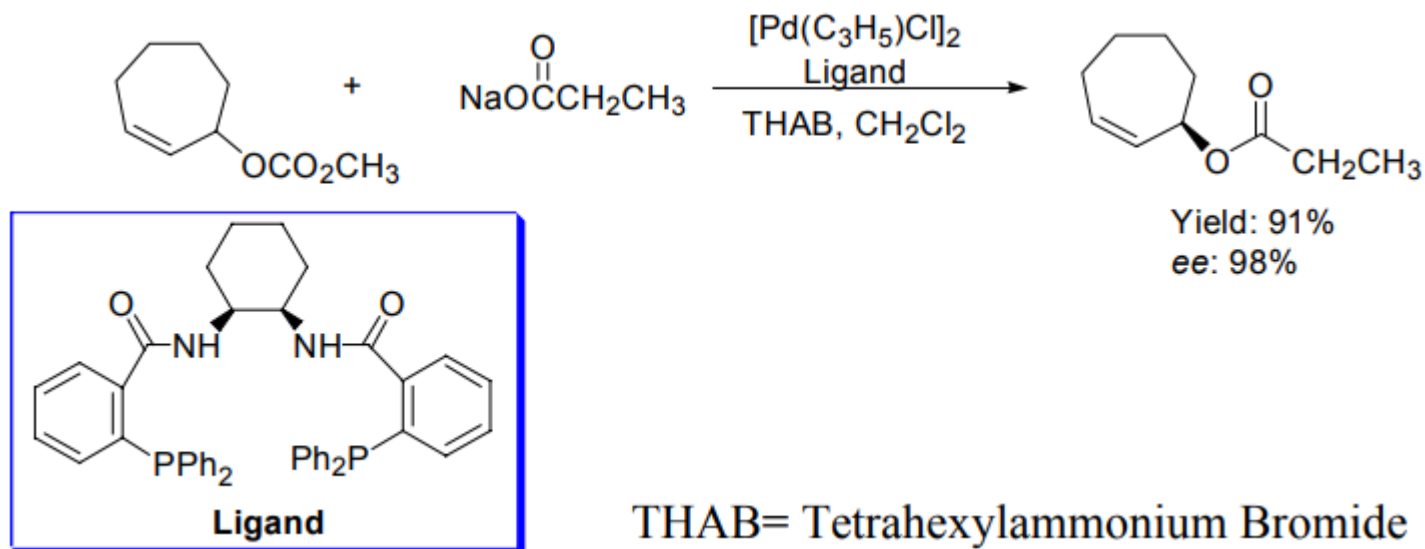
Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1977**, 99, 1649-1651

Asymmetric Catalytic Tsuji-Trost-type Reaction



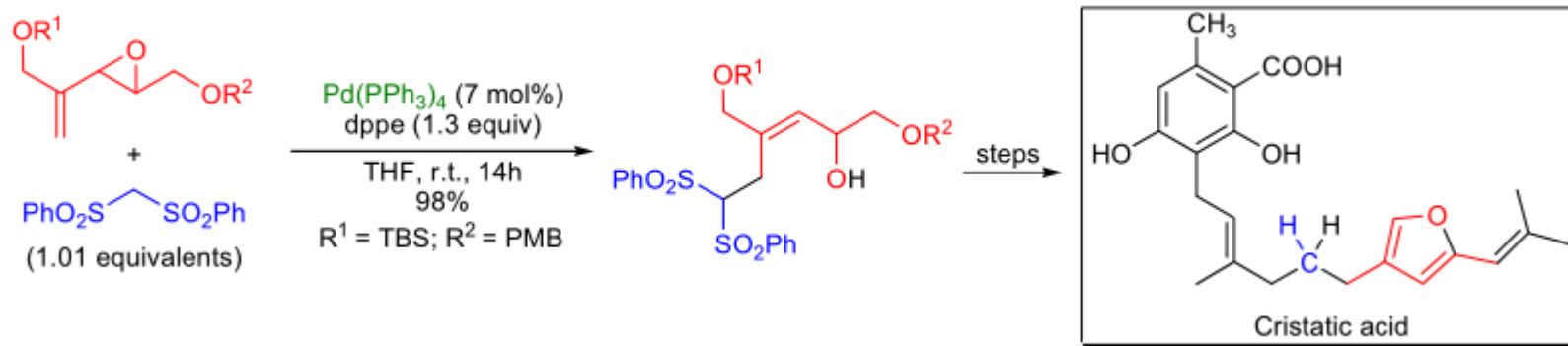
Wimmer, P.; Widhalm, M. *Tetrahedron Asym.* **1995**, 6, 657-660

Asymmetric Catalytic Tsuji-Trost-type Reaction

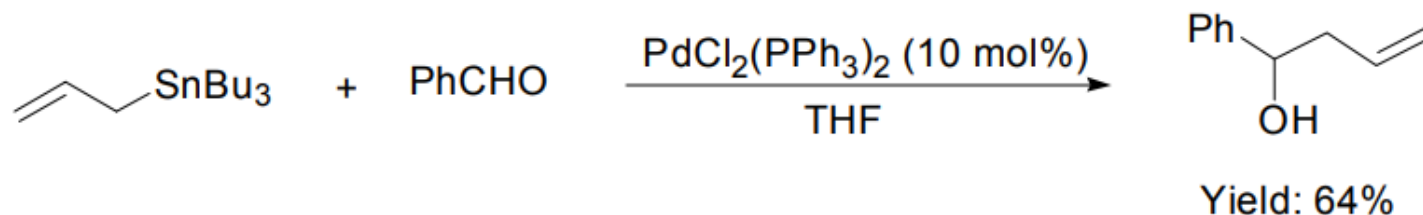


Trost, B. M.; Organ, M. G. *J. Am. Chem. Soc.* **1994**, 116, 10320-10321

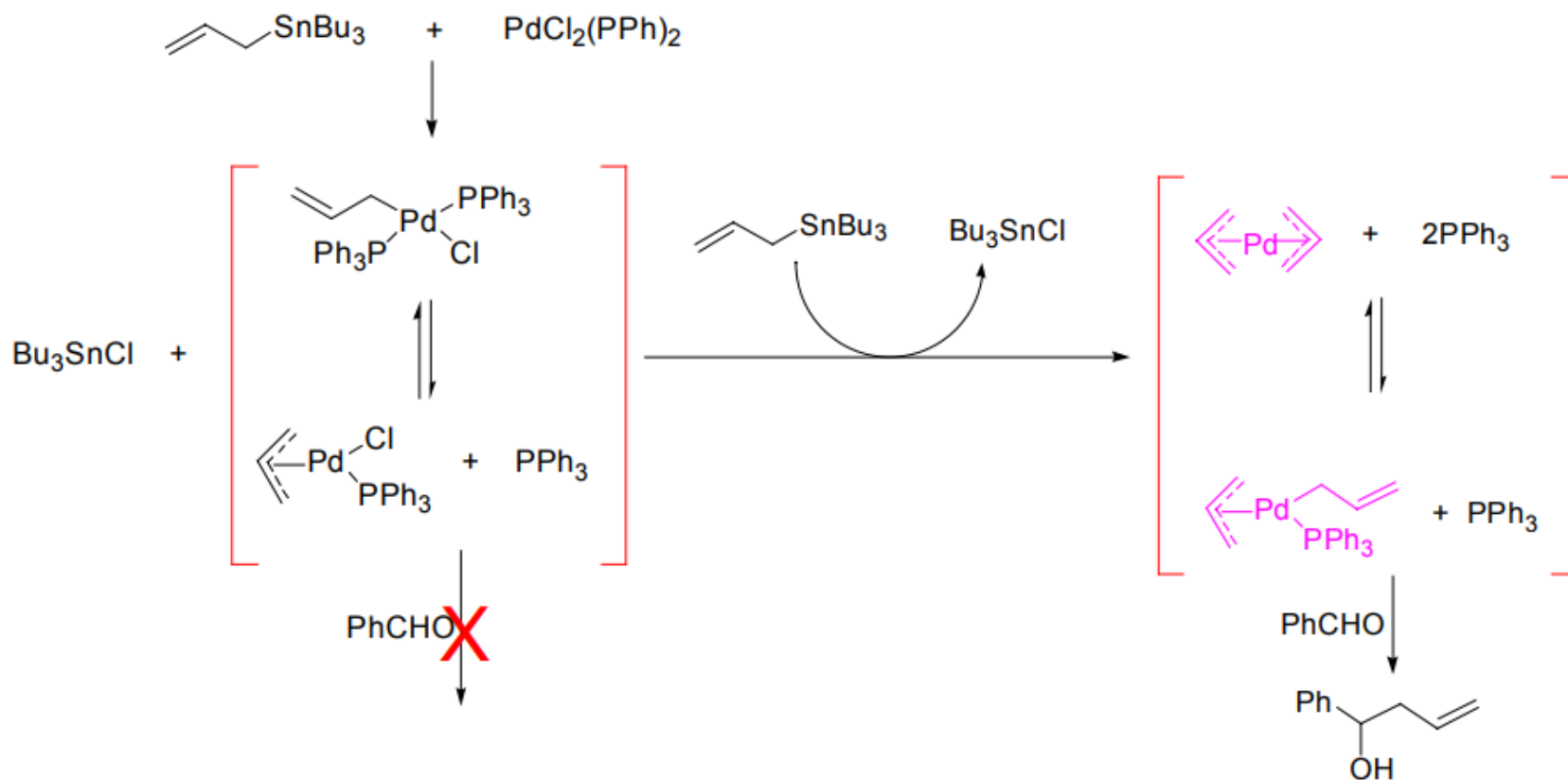
Synthetic Applications



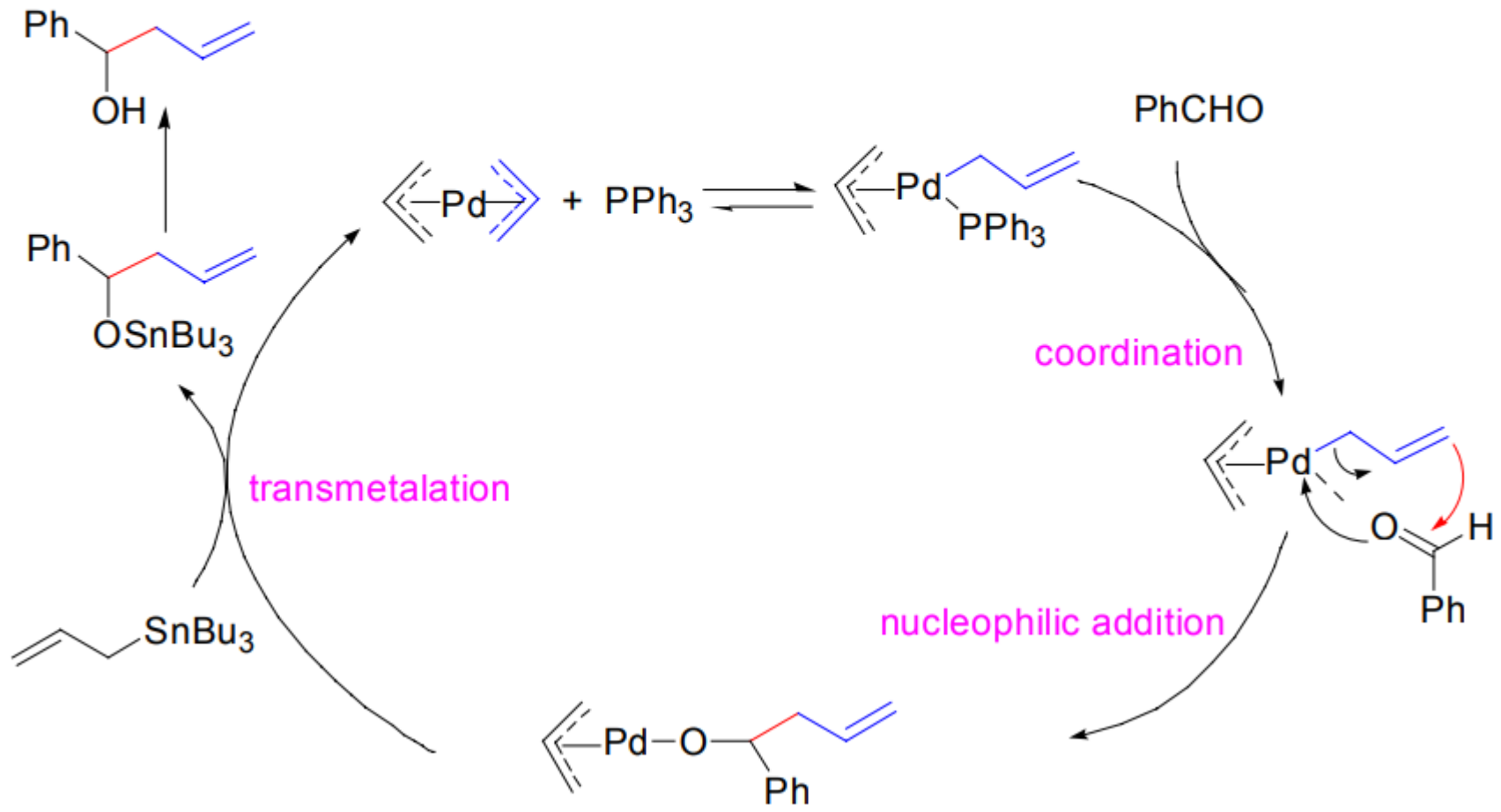
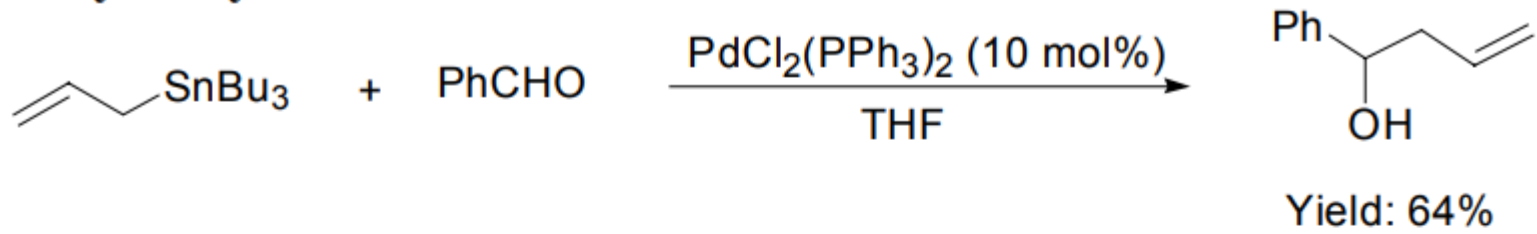
Discovery of Bis- π -allylpalladium Complexes

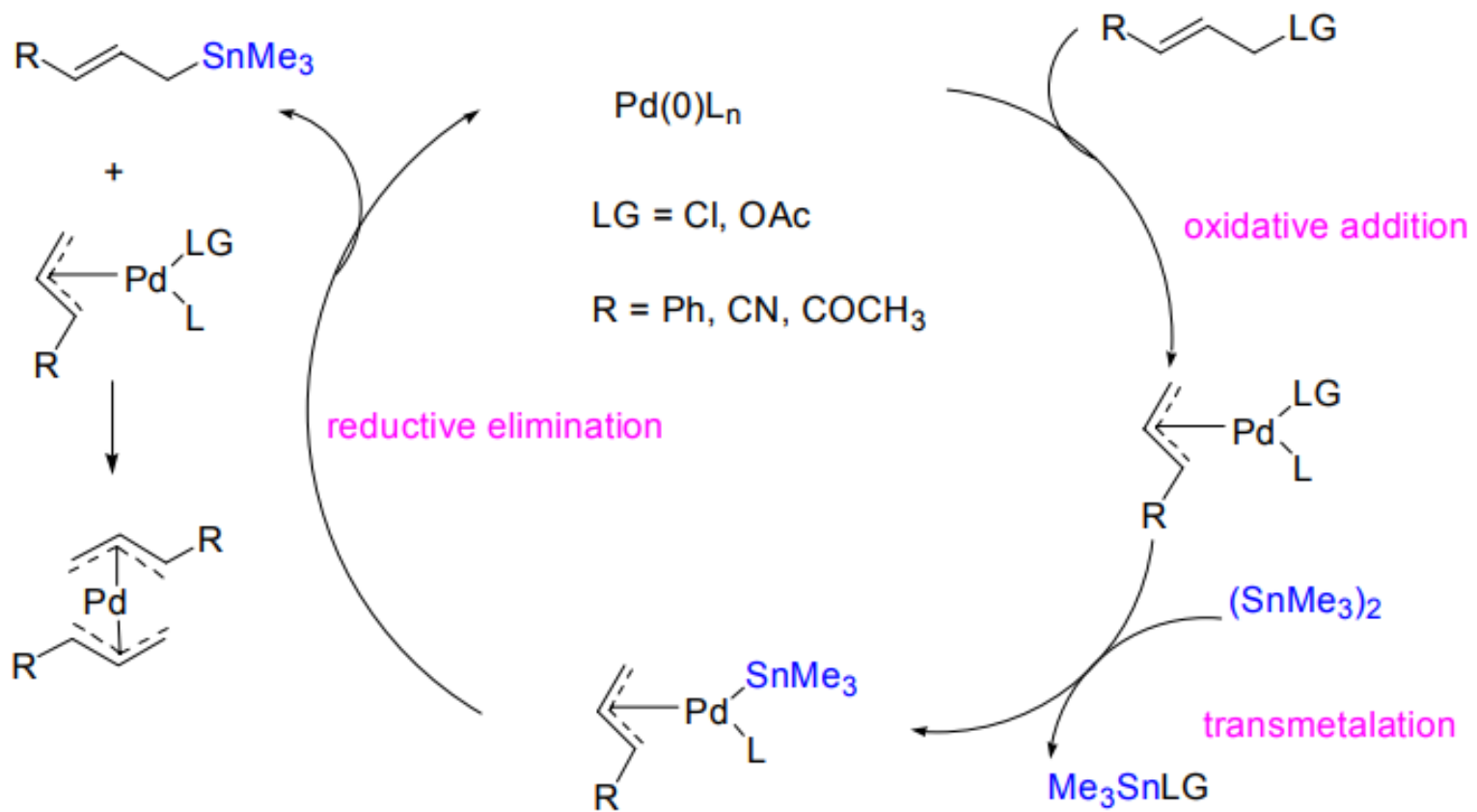


Mechanistic Study



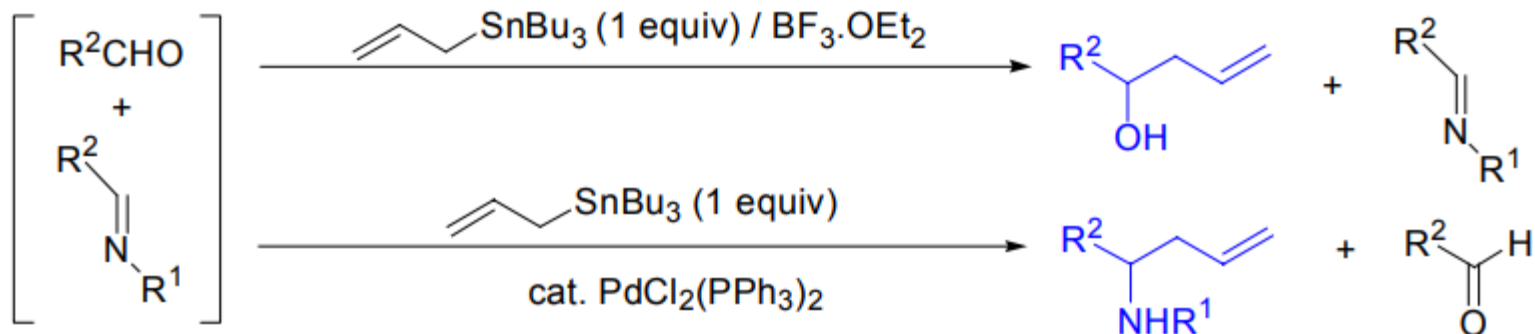
Catalytic Cycle

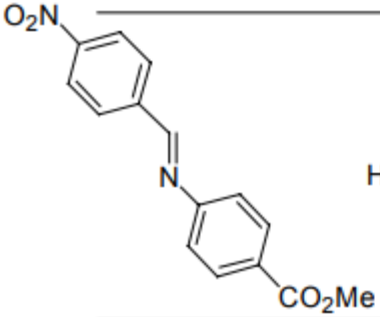
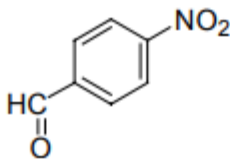
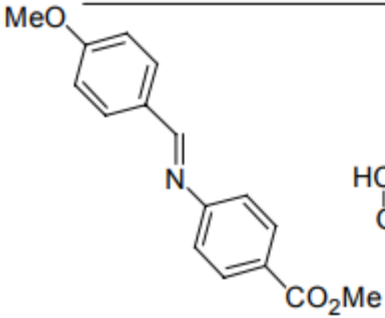
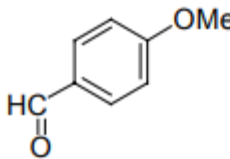




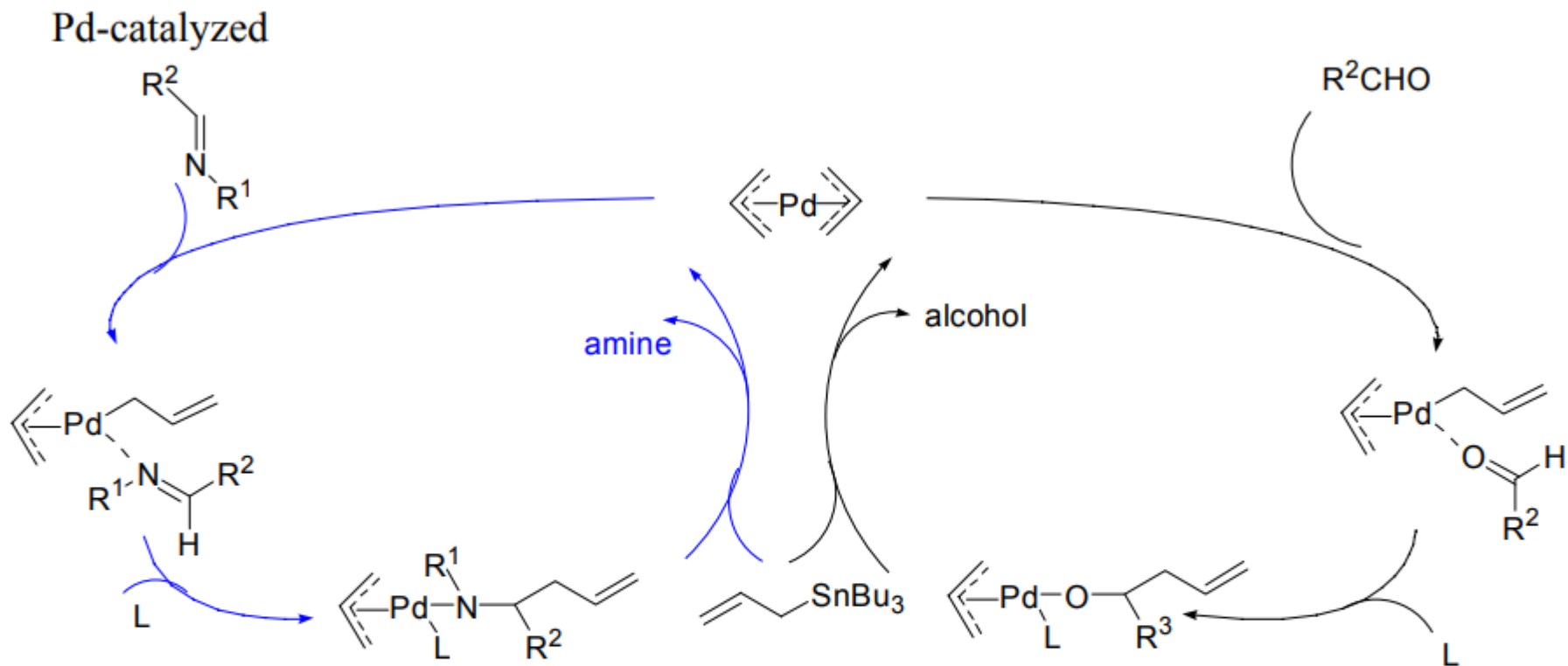
Wallner, O. A.; Szabo, K. *J. Org. Lett.* **2002**, 4, 1563-1566

Chemoselective Allylation of Imines in the Presence of Aldehydes

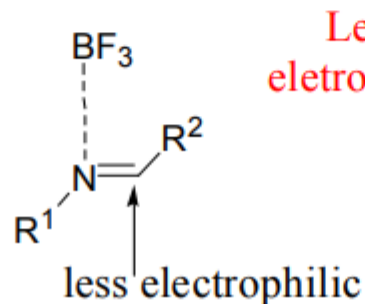


imine	aldehyde	condition	yield(%)	ratio of amine/alcohol
		Pd-catalyzed	90	90 : 10
		Lewis Acid Promoted	95	10 : 90
		Pd-catalyzed	99	97 : 3
		Lewis Acid Promoted	96	<1 : 99

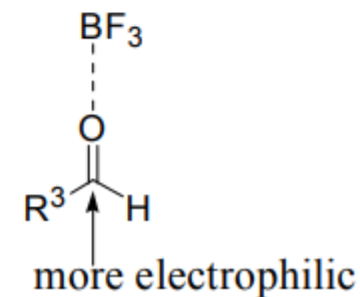
Chemoselective Allylation of Imines in the Presence of Aldehydes



Lewis Acid Promoted



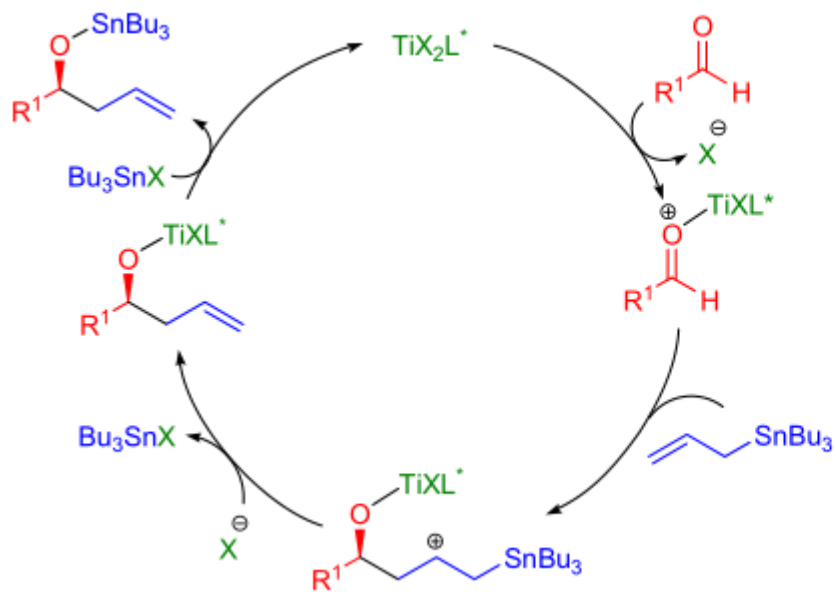
Lewis acid activates both electrophiles in the same manner



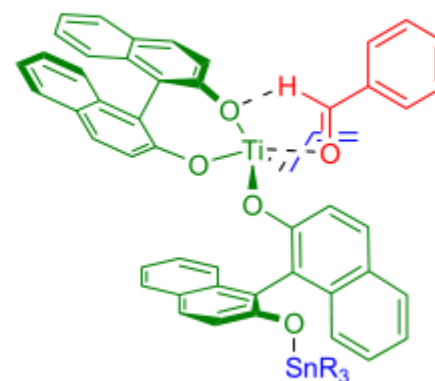
KECK ASYMMETRIC ALLYLATION



R^1 = alkyl, aryl, alkenyl; R^2 = alkyl, O-alkyl; **Mikami's catalyst:** $\text{TiCl}_2(\text{O}i\text{-Pr})_2$ + (*S*)-BINOL (0.3 equiv) + 4Å MS in CH_2Cl_2 , toluene, 1h, r.t.; **Keck's catalyst:** $\text{Ti}(\text{O}i\text{-Pr})_4$ + (*R*)-BINOL (2 equiv) + 4Å mol sieves in CH_2Cl_2 , 1h, r.t.; **Tagliavini's catalyst:** $\text{TiCl}_2(\text{O}i\text{-Pr})_2$ + (*S*)-BINOL (slight excess) + 4Å mol. sieves in CH_2Cl_2 , 2h, r.t.;

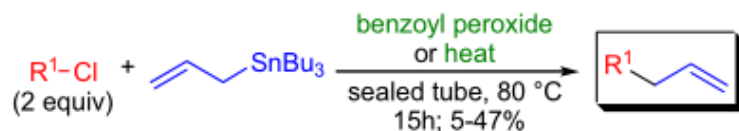


Corey's stereochemical model:



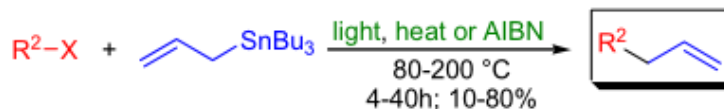
KECK RADICAL ALLYLATION

Kosugi's procedure (1973):



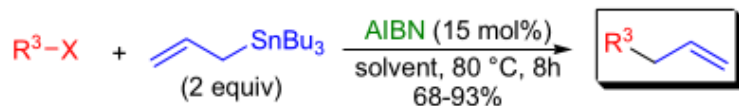
$R^1 = -\text{CCl}_3, -\text{CHCl}_2, -\text{CH}_2\text{CO}_2\text{Me}, -\text{CH}_2\text{CCl}_3$

Grignon's procedure (1973, 1975):



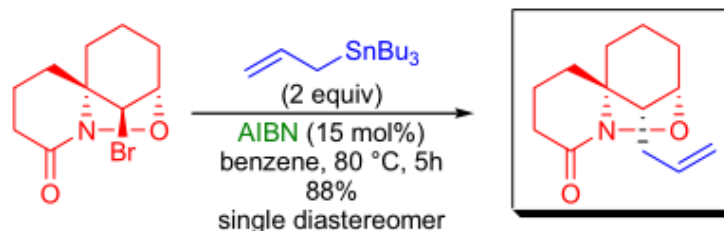
$R^2 = -\text{CCl}_3, -\text{CHCl}_2, -\text{CH}_2\text{Cl}, -\text{CH}_2\text{CO}_2\text{Et}, -\text{CCl}_2\text{CO}_2\text{Et}, -\text{CCl}_2\text{CHO}, -\text{CBr}_2\text{CHO}, -\text{CH}(\text{CH}_3)\text{CO}_2\text{Me}, n\text{-propyl}, i\text{-Pr}, t\text{-Bu}, \text{allyl}, t\text{-butylcyclohexyl}, \text{aryl}; X = \text{Cl}, \text{Br}$

Keck's general process (1982):

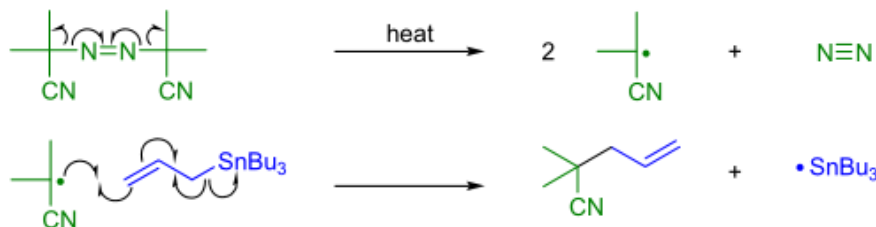


$R^3 = 1^\circ, 2^\circ, \text{ and } 3^\circ \text{ alkyl}; X = \text{Cl}, \text{Br}, \text{SePh}, \text{thioacylimidazole};$
solvent = benzene, toluene;

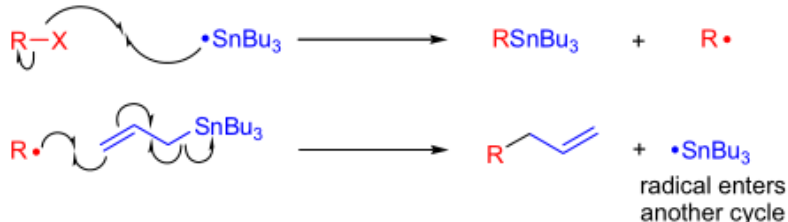
Keck's specific example (1982):



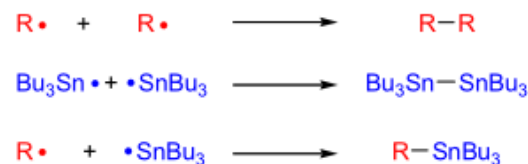
Initiation step:



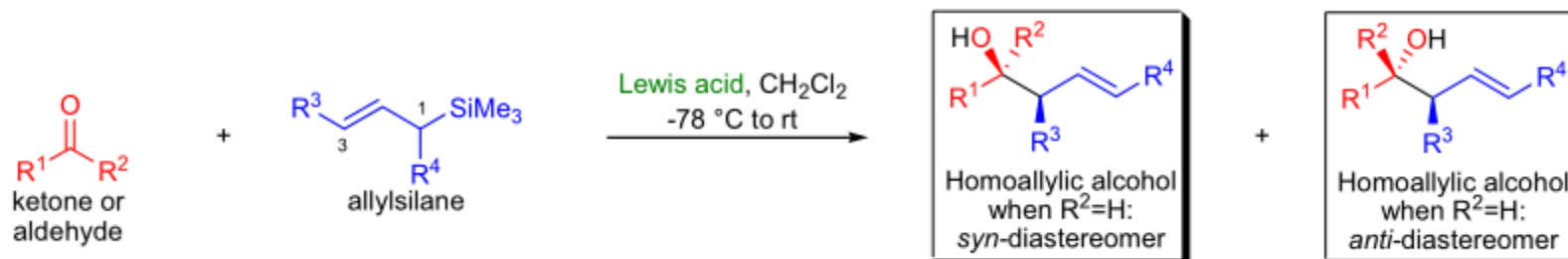
Propagation step:



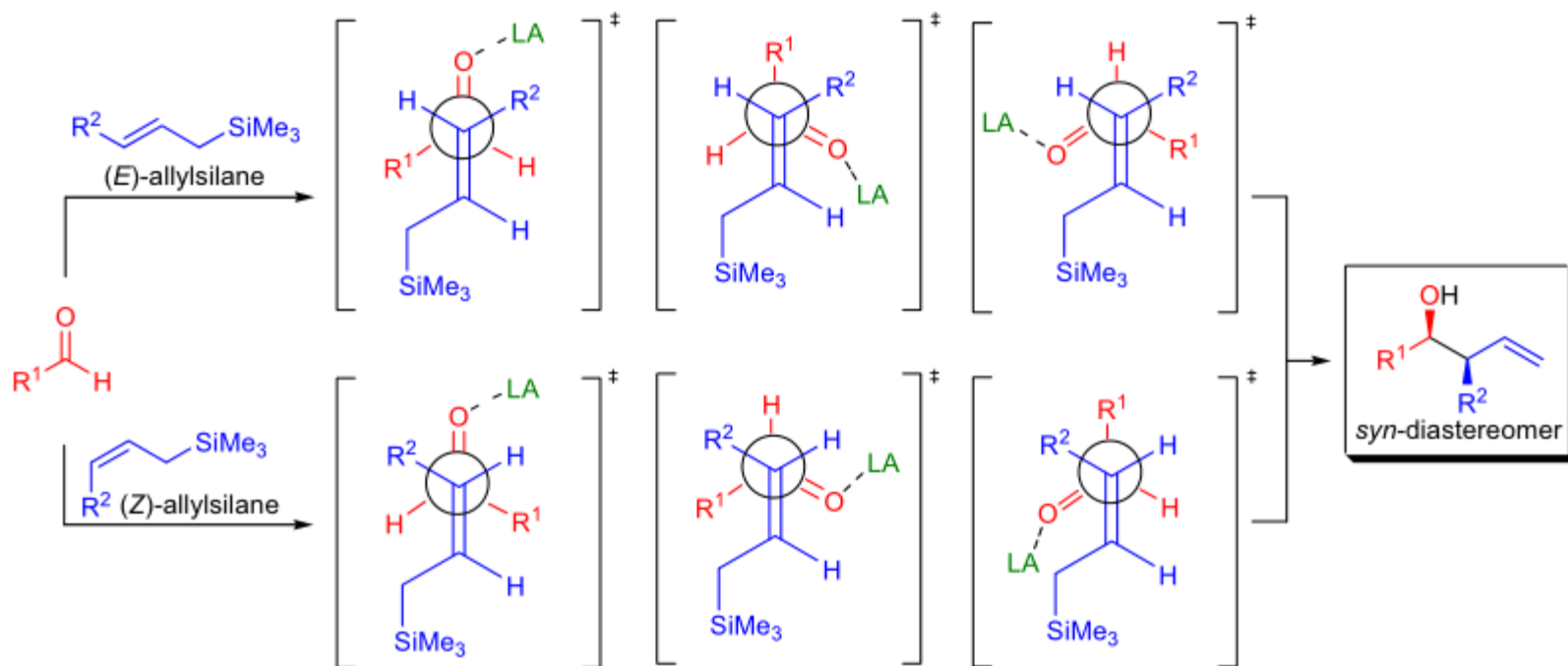
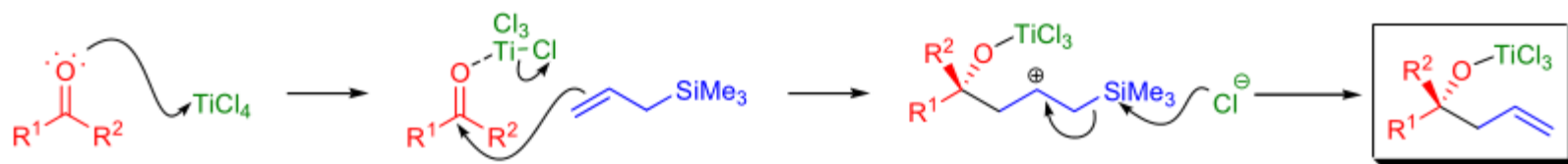
Termination steps



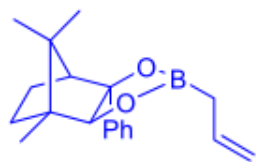
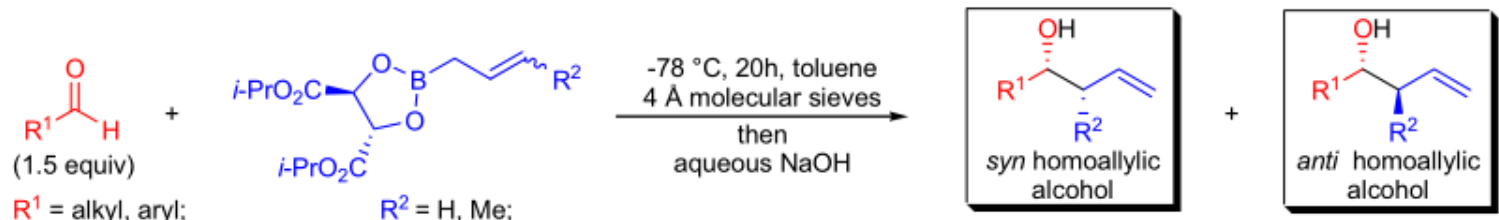
SAKURAI ALLYLATION



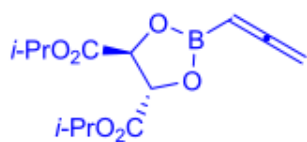
R¹ = alkyl, aryl; R² = H, alkyl, aryl; R³ and R⁴ = H, alkyl, aryl; Lewis acid = TiCl₄, BF₃·OEt₂, SnCl₄, EtAlCl₂



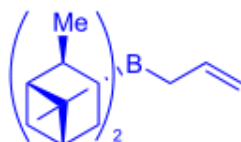
ROUSH ASYMMETRIC ALLYLATION



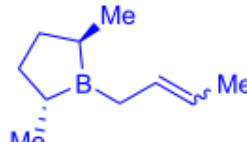
Hoffmann (1978)



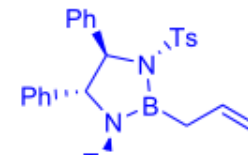
Yamamoto (1982)



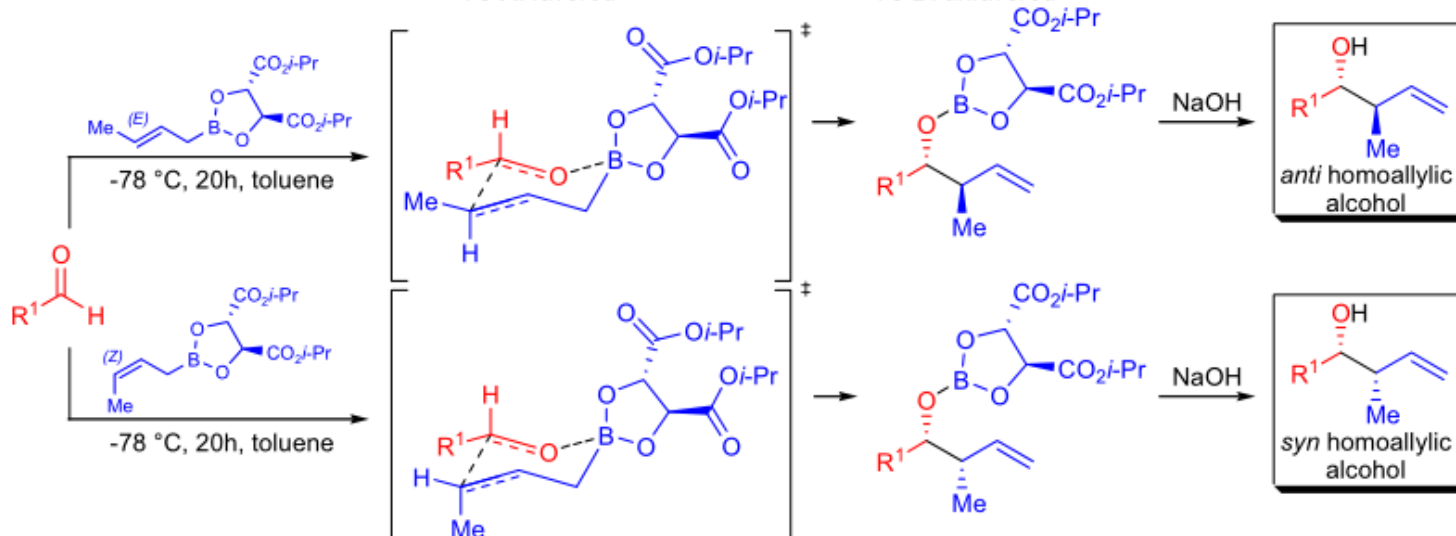
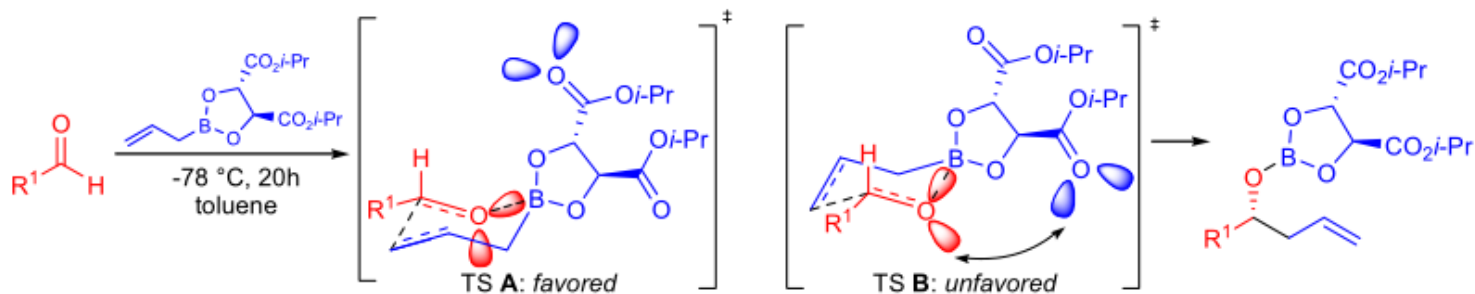
Brown (1983)



Masamune (1987)



Corey (1989)



Krische allylation

