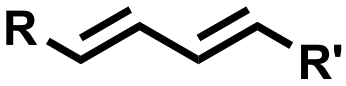
Nobel Lecture, December 8, 2010

Cross-Coupling Reactions of Organoboranes:

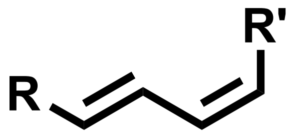
An Easy Way for Carbon-Carbon Bonding

Akira Suzuki

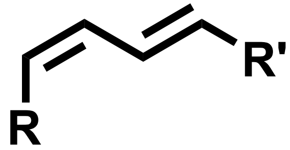
Conjugated Alkadienes



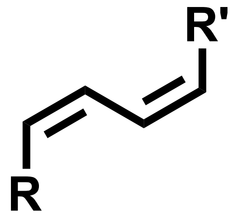
trans-trans



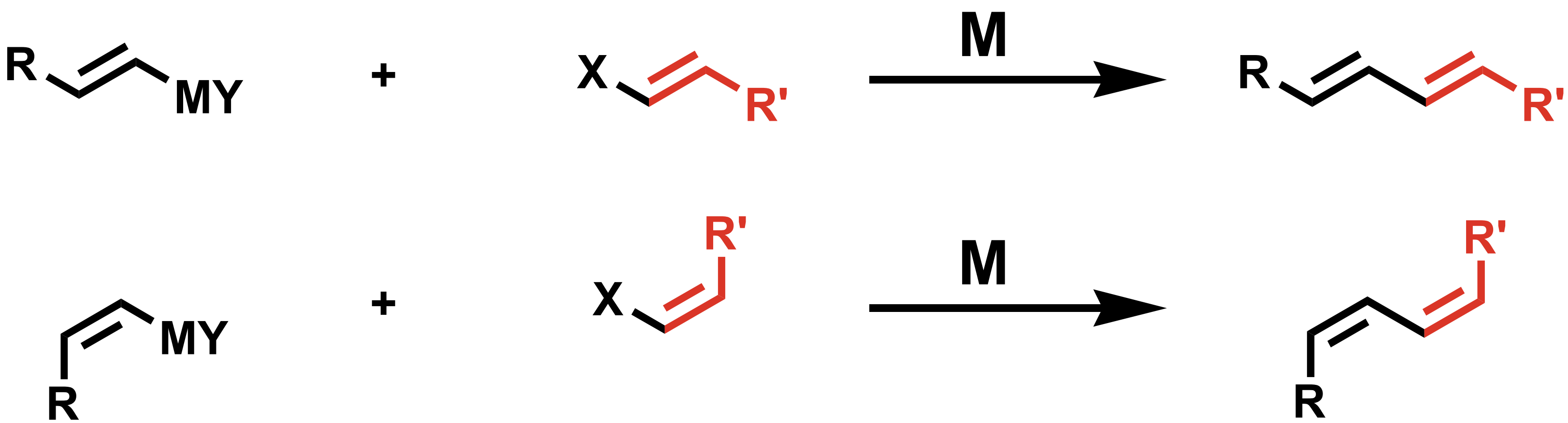
trans-cis



cis-trans

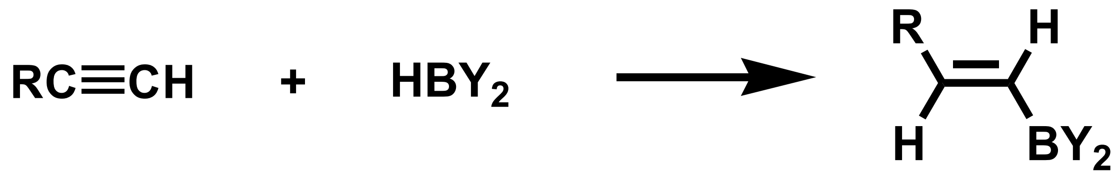


cis-cis

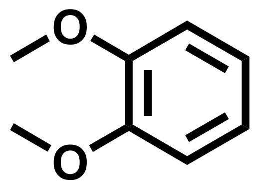


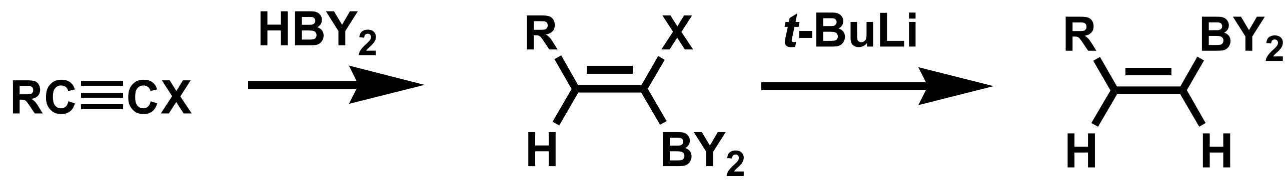
M : transition metal catalyst

Syntheses of (E)- and (Z)-1-Alkenylboranes



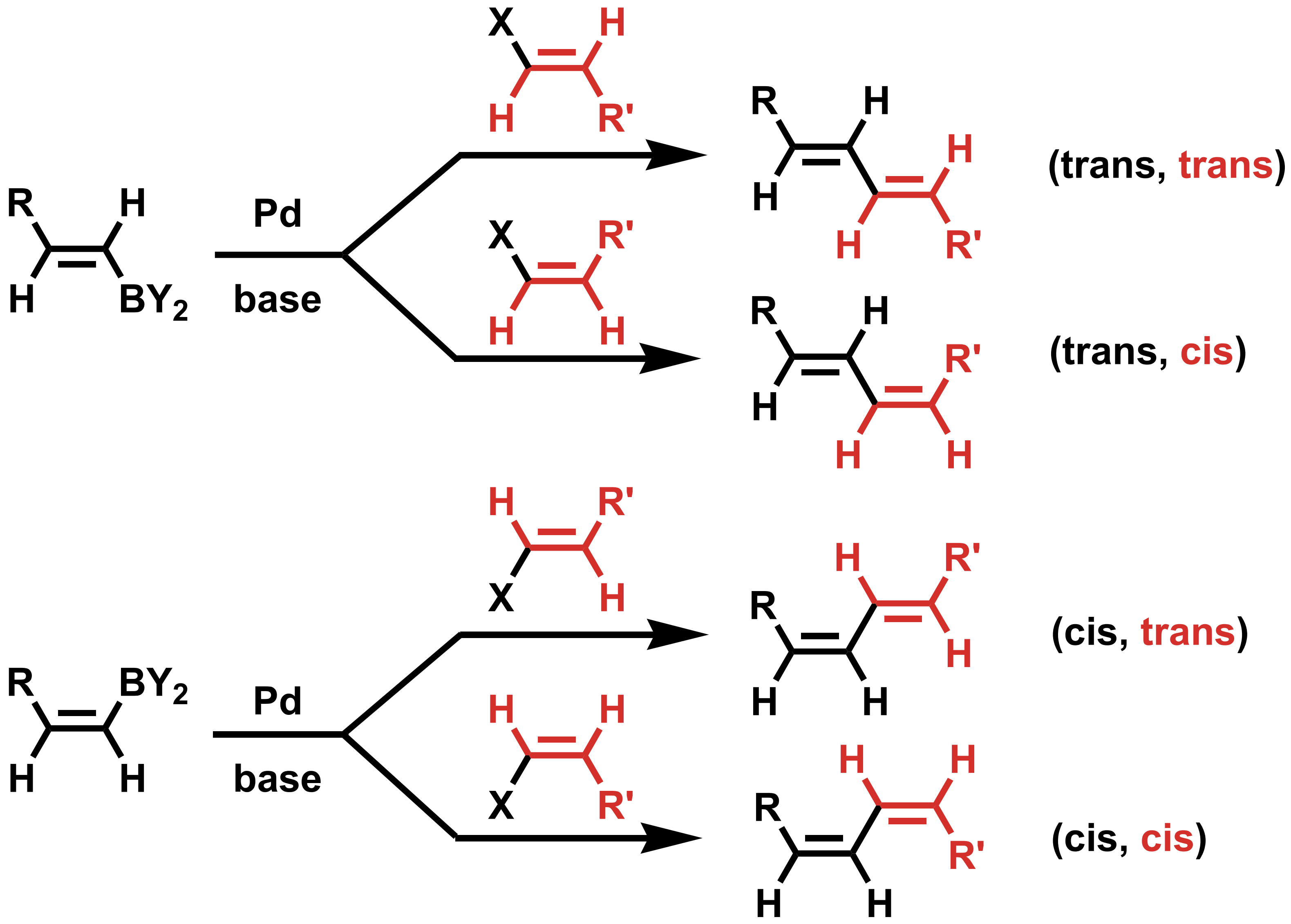
trans > 99 %

Y_2 = $(Siamyl)_2$, 

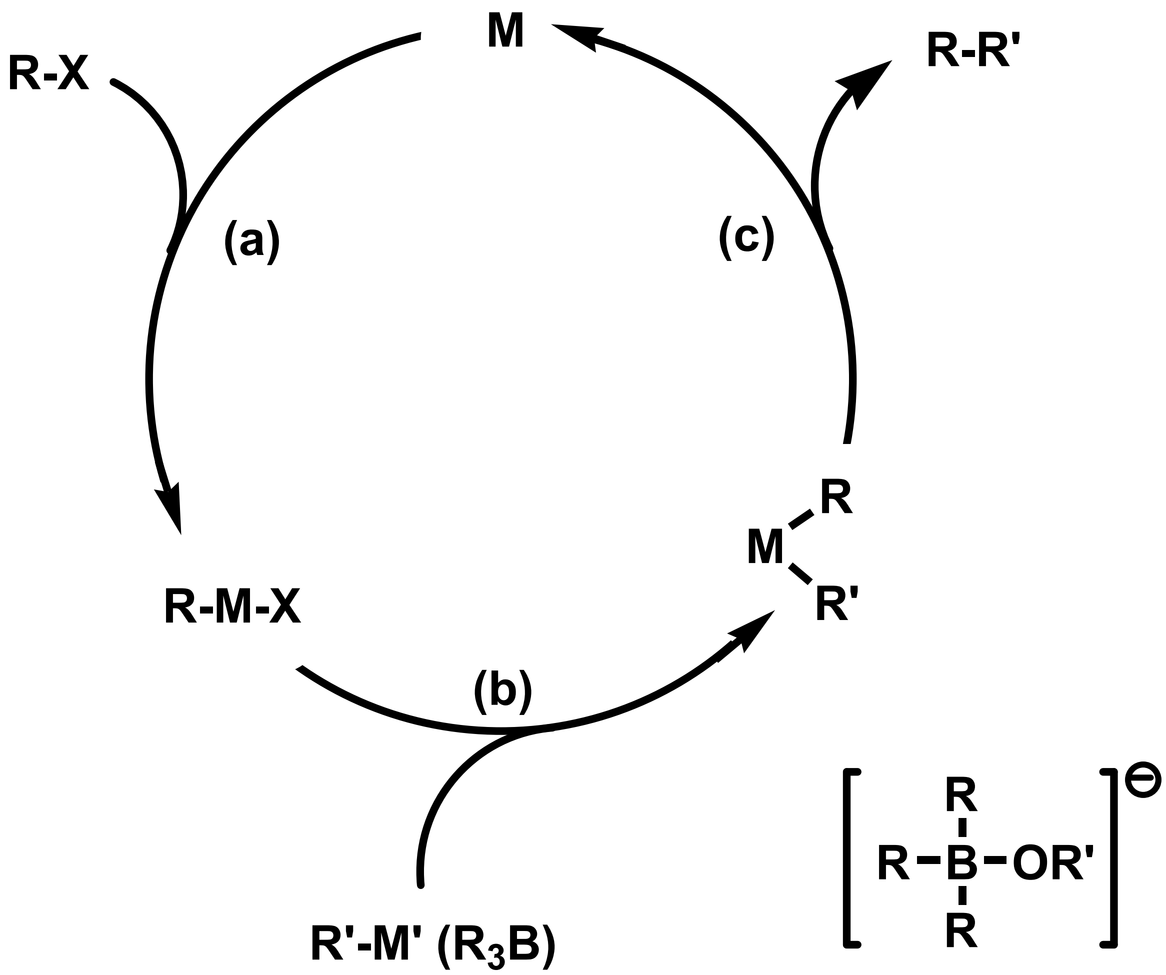


cis > 98 %

X = I or Br   Y = Siamyl, Cyclohexyl

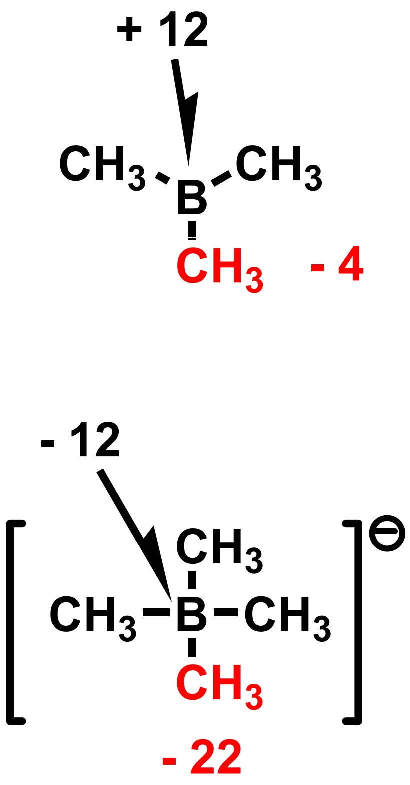

Pd
base
(trans, trans)
(trans, cis)
(cis, trans)
(cis, cis)

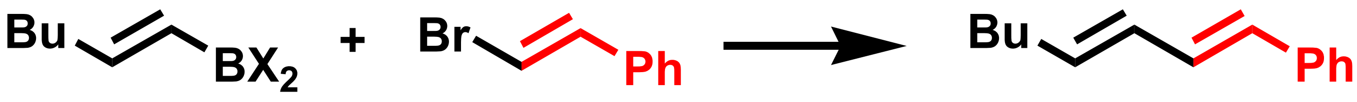
Common Catalytic Cycle Involving Sequential Oxidative Addition (a), Transmetalation (b), and Reductive Elimination (c)



Atomic charge in 0.01 e.u.

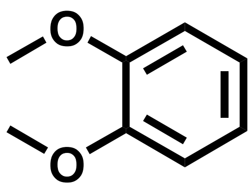
(Gropen & Haaland, 1973)

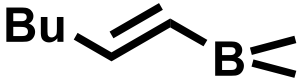
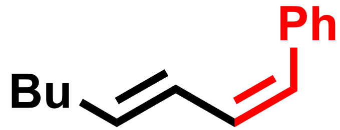
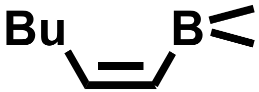
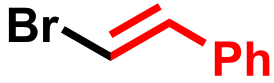
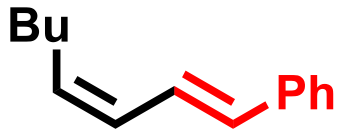
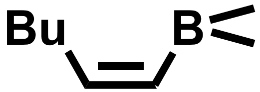
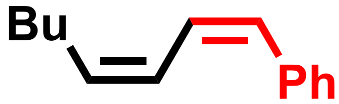
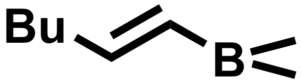
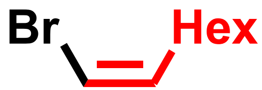
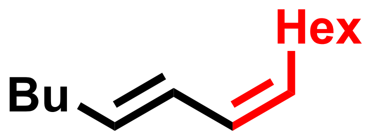
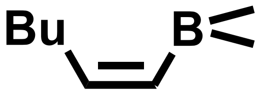
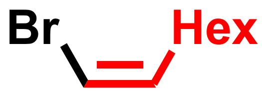
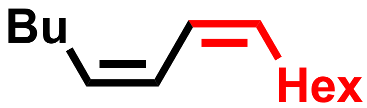
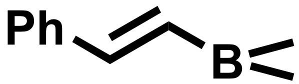
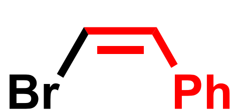
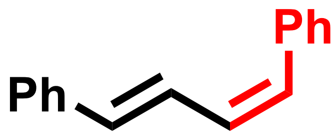




1 2 3

$1^{a)}$	Catalyst[b)] (mol %)	Base (equiv / 2)	Solvent	React. time (h)	Yield (%) of 3
1b	PdL_4 (3)	None	THF	6	0
1b	PdL_4 (3)	None	Benzene	6	0
1a	PdL_4 (3)	2M NaOEt (2)-EtOH	THF	2	73
1b	PdL_4 (3)	2M NaOEt (2)-EtOH	THF	4	78
1b	PdL_4 (1)	2M NaOEt (2)-EtOH	Benzene	2	86

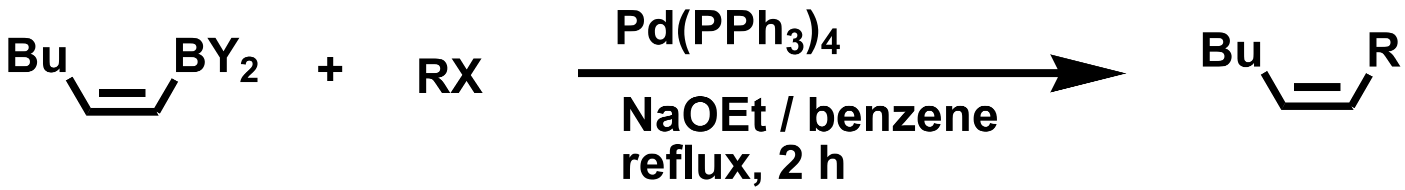
a) 1a, X_2 = $(Sia)_2$ 1b, X_2 =  b) L = PPh_3

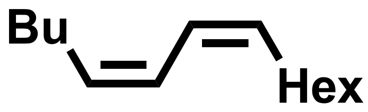
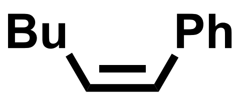
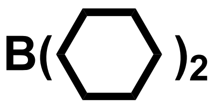
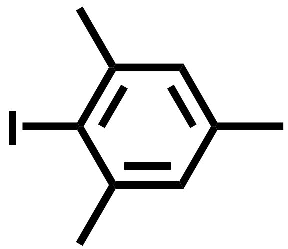
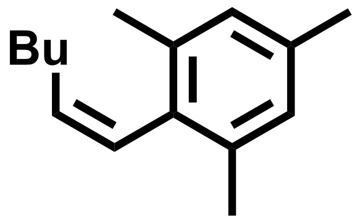
1-Alkenylborane		1-Alkenyl Bromide	Product	Yield (%) [Purity (%)]
	b)			86 [98]
	a)			49 [99]
	a)			42 [89]
	b)			88 [99]
	a)			49 [98]
	b)			89 [98]

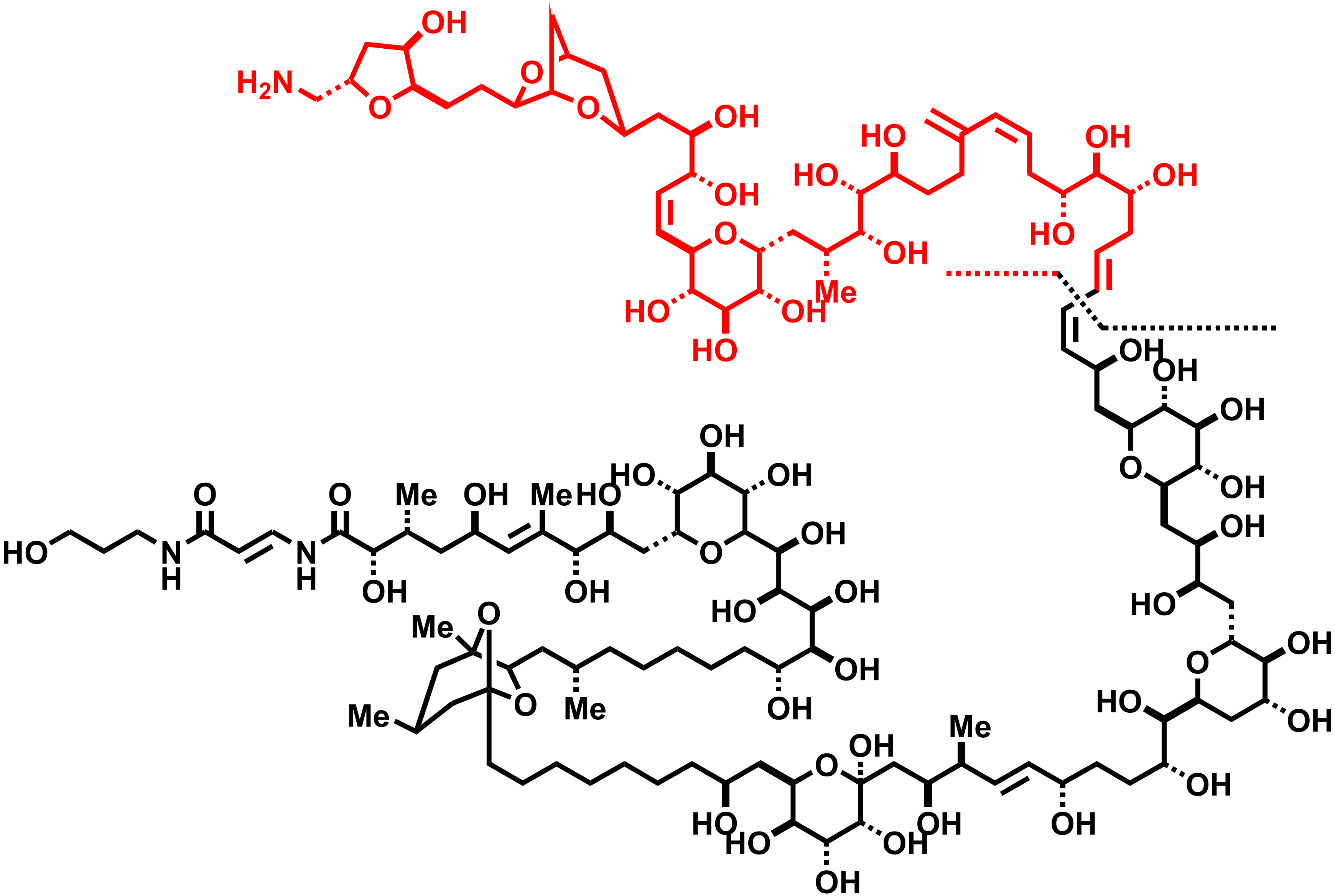
Reaction conditions: 1-3 mol % of $Pd(PPh_3)_4$ / NaOEt / Benzene / Reflux 2h

a) Disiamyl b) 1,3,2-Benzodioxaboryl

N-8



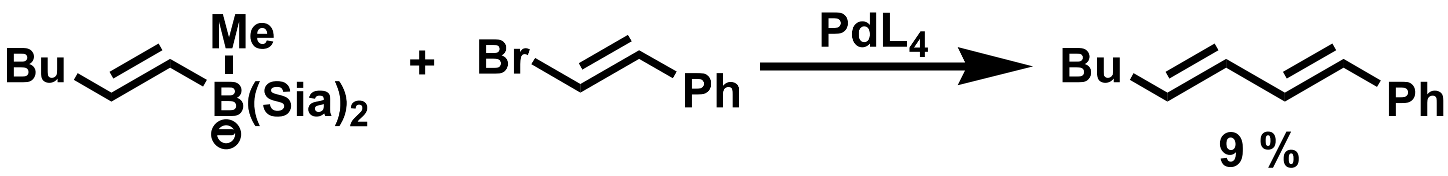
BY_2	RX	Product	Yield (%)	Purity (%)
$B(Sia)_2$			49	>98
$B(OPr^i)_2$			87	>99
$B(Sia)_2$	PhI		58	>94
			49	>83
$B(OPr^i)_2$			98	>97
$B(Sia)_2$			54	>92
$B(OPr^i)_2$			87	>99

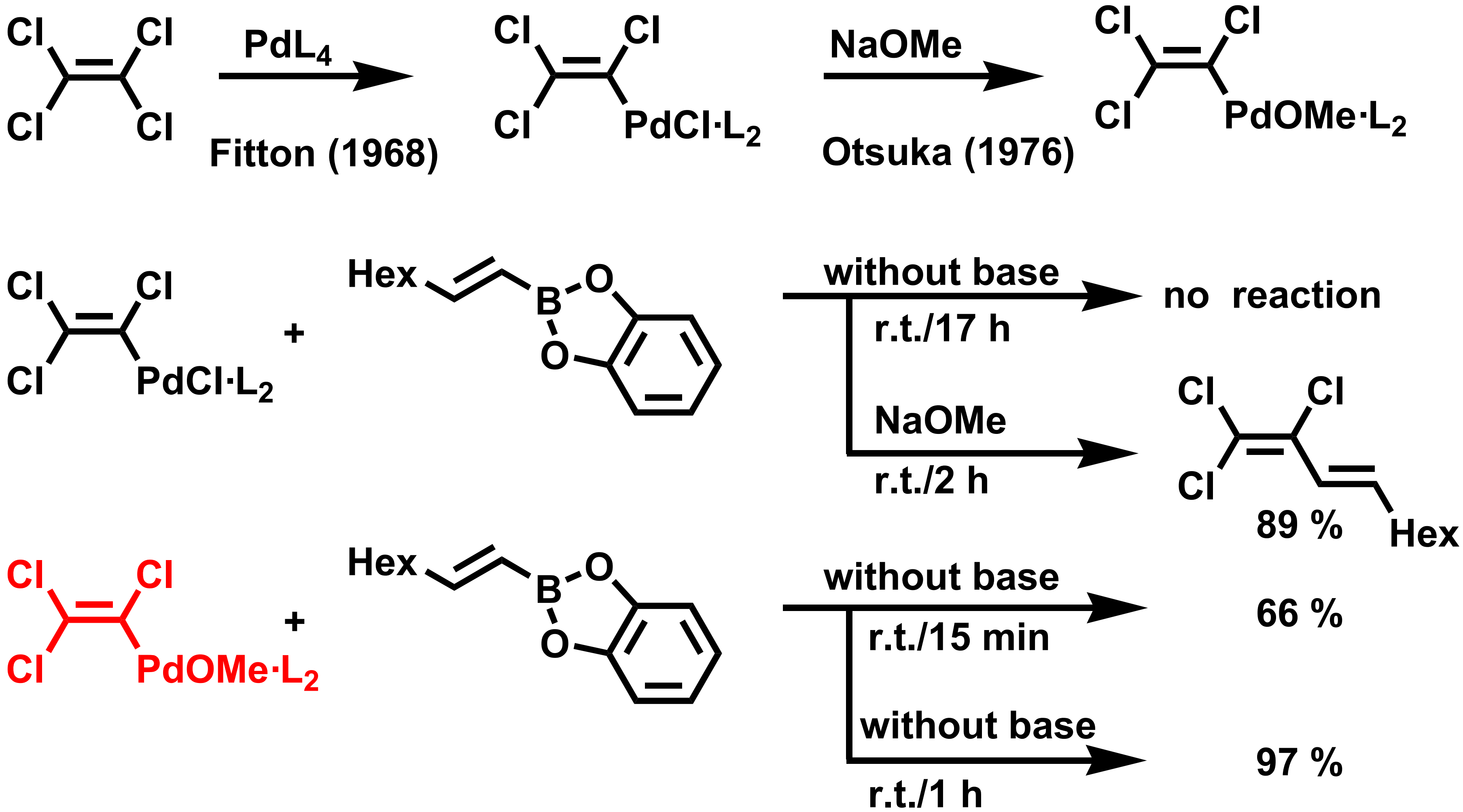


"Palytoxin" $C_{129}H_{223}N_3O_{54}$ (MW. 2678.6)

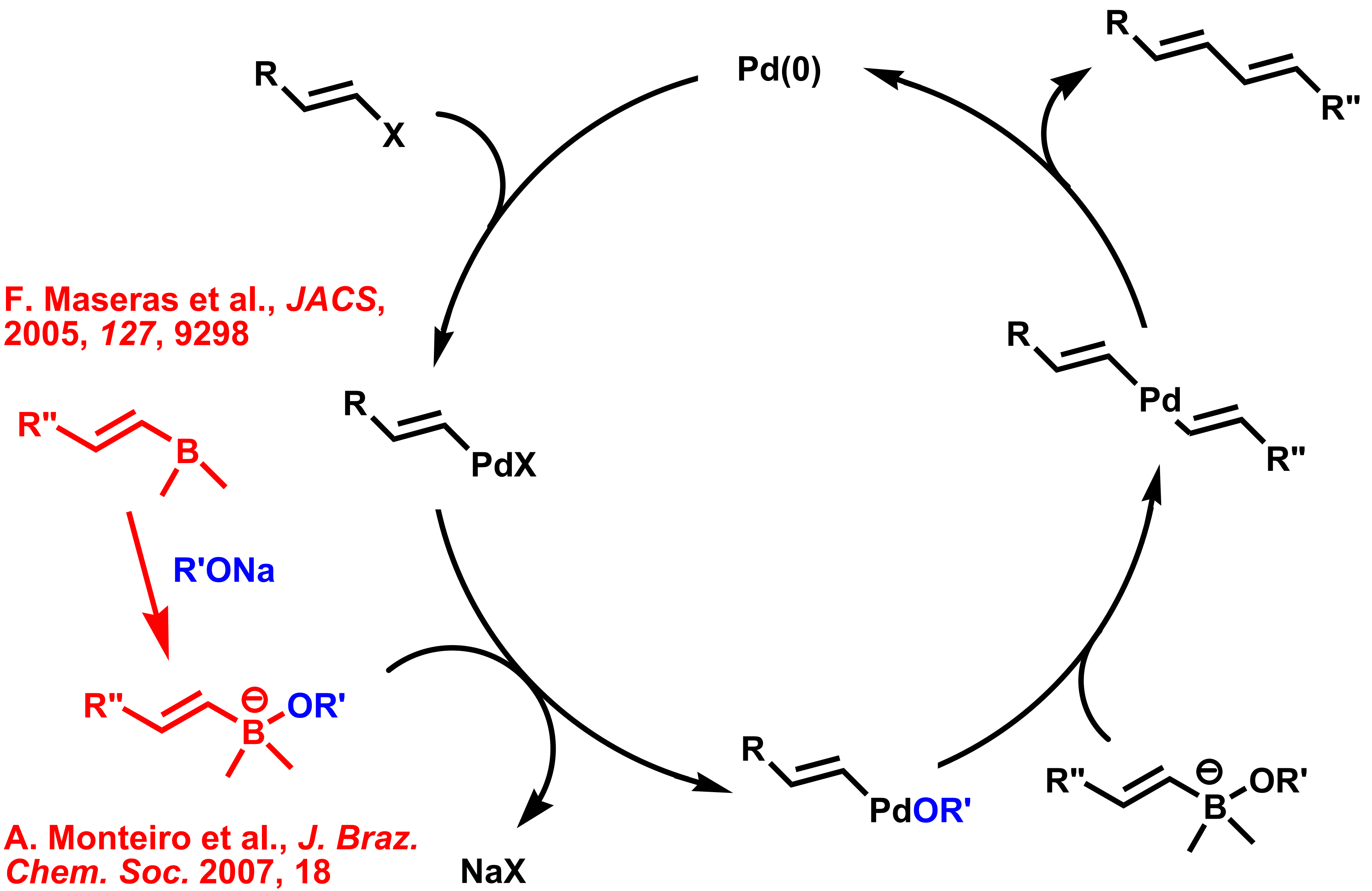
Synthesis: Kishi et al., *J. Am. Chem. Soc*, 1989, *111*, 7525, 7530

Reaction Mechanism:

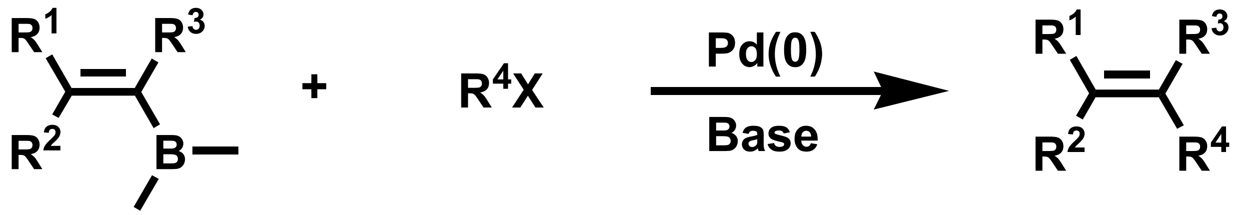




Catalytic Formulation of the Vinyl-Vinyl Cross-Coupling



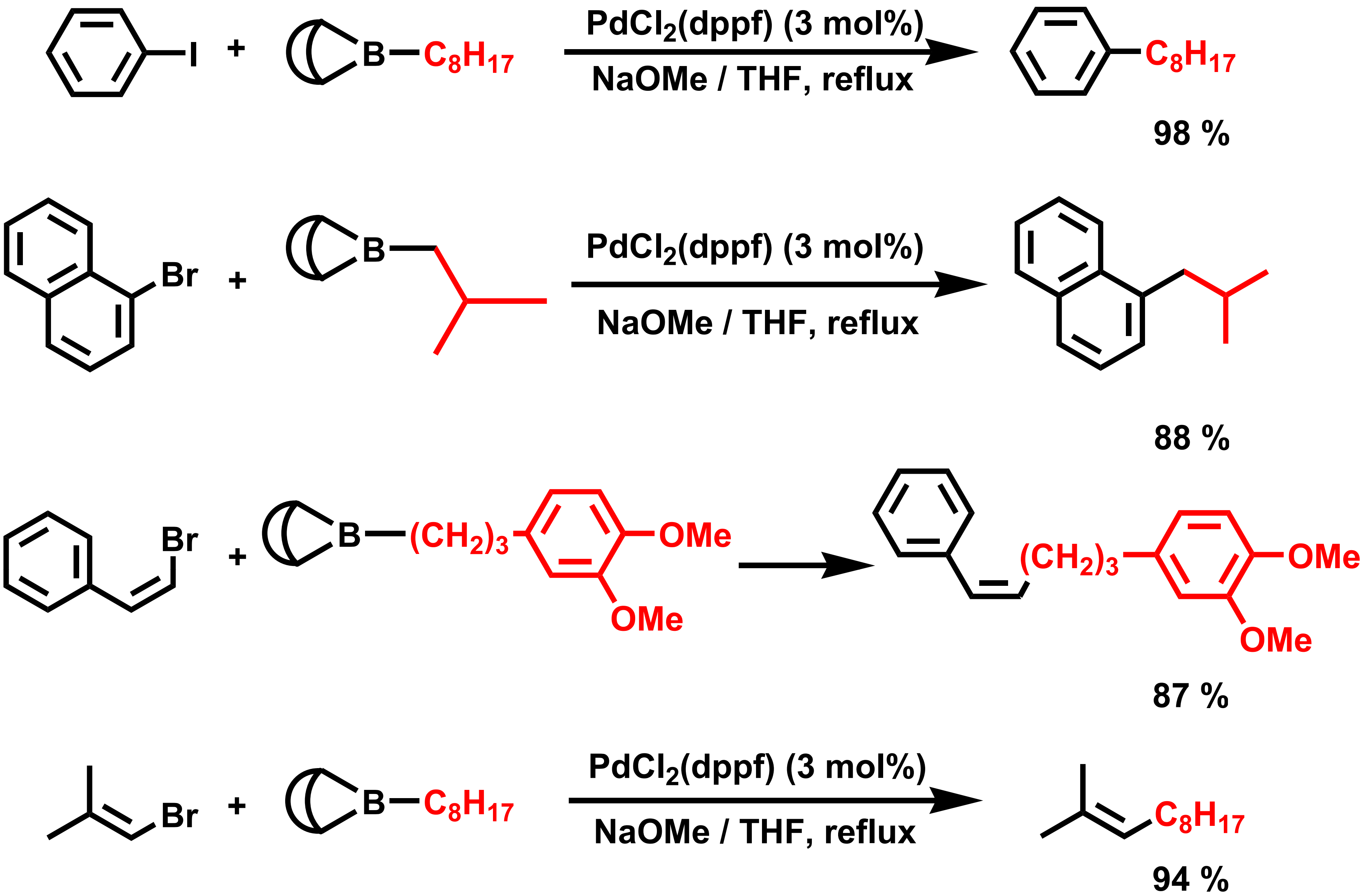
Reaction of B-Alkylboranes



R4 : 1-Alkenyl
Aryl
1-Alkynyl
Allyl
Benzyl

R : Alkyl

N-13

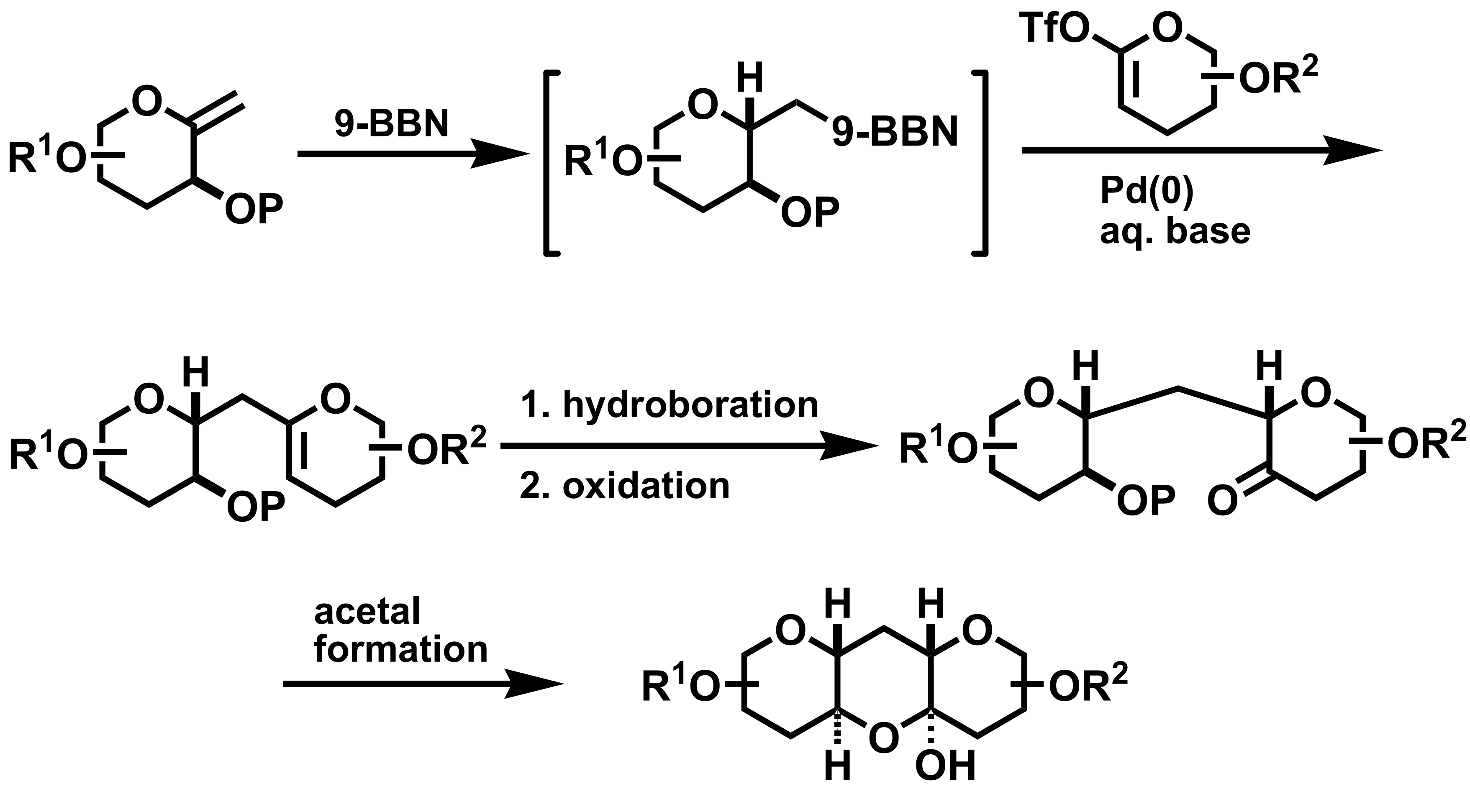


PdCl2(dppf) (3 mol%)
NaOMe / THF, reflux
B
C8H17
98 %
Br
88 %
(CH2)3
OMe
OMe
87 %
94 %

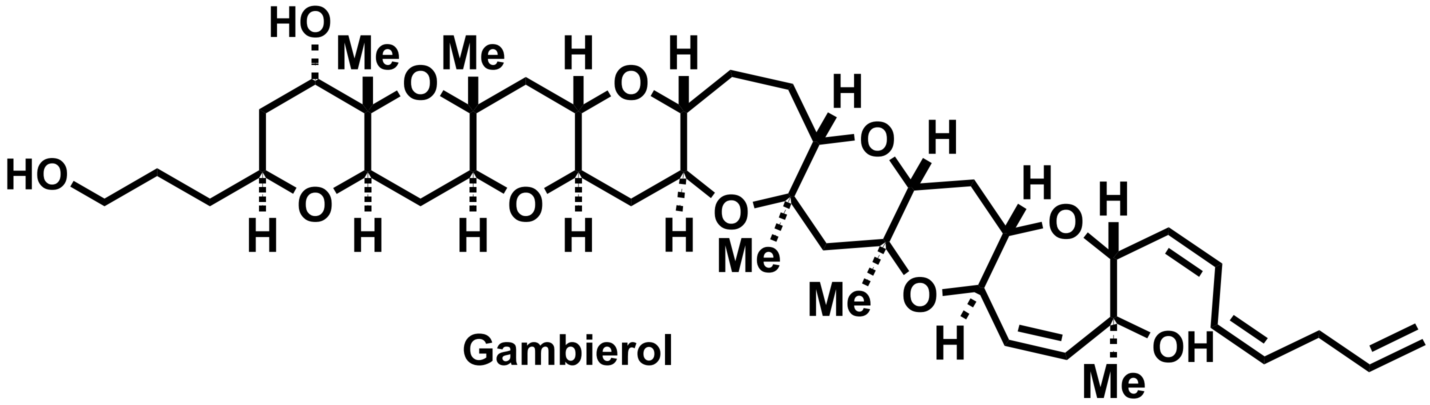
Alkyl-Vinyl Coupling:

Total Synthesis of Polycyclic Ether Natural Product

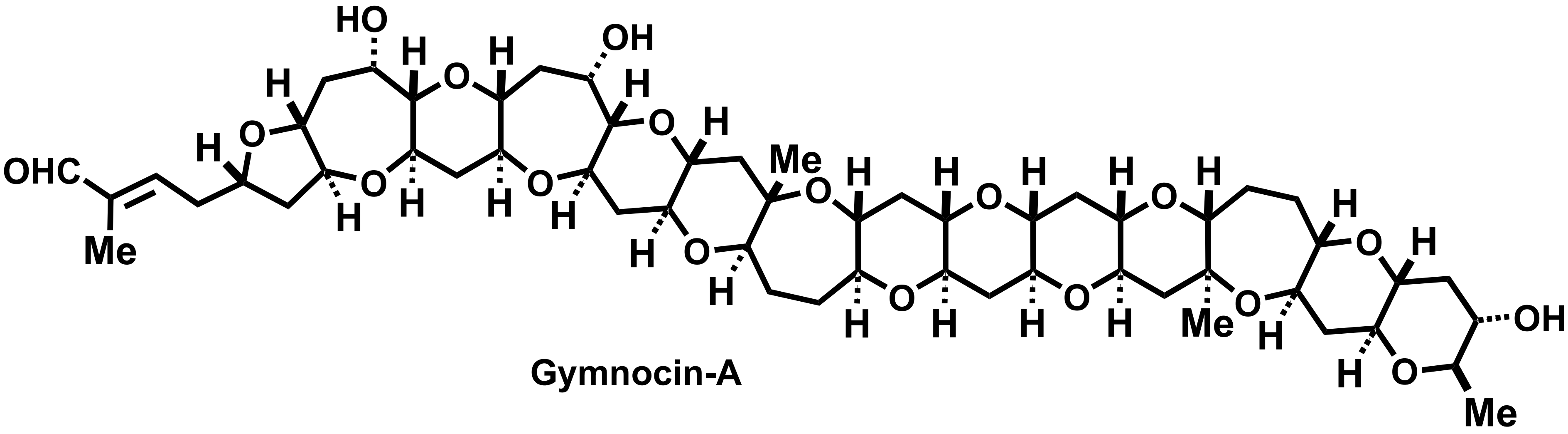
M. Sasaki, *Bull. Chem. Soc. Jpn.* 2007, *80*, 856



Polycyclic Ether Marine Natural Products:

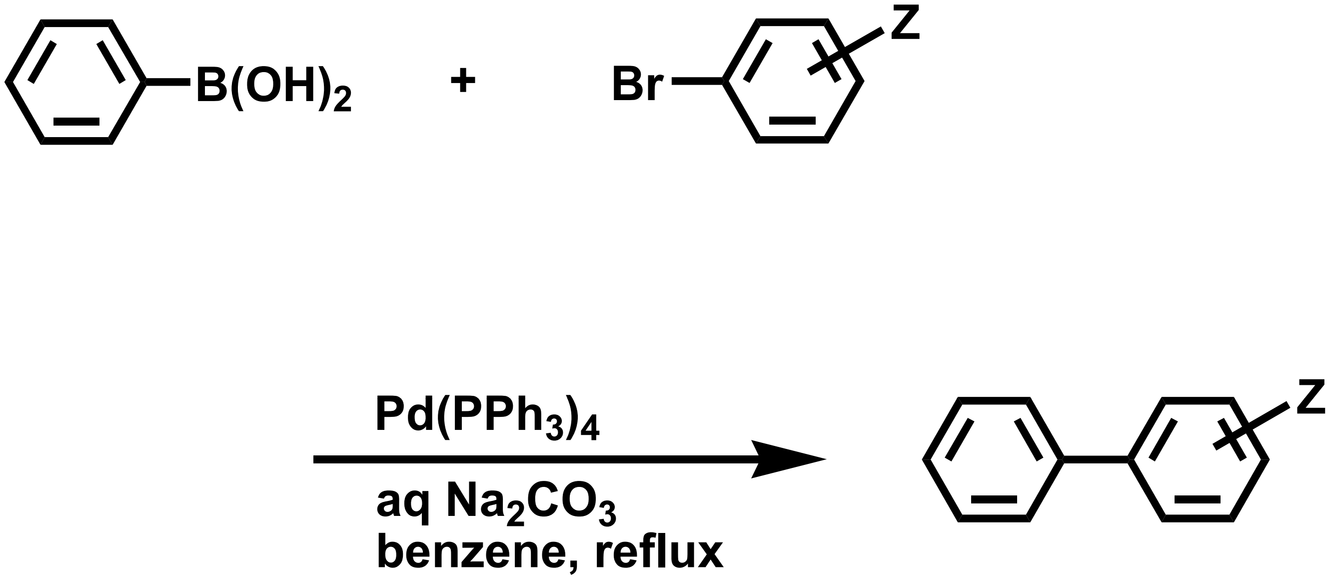


Gambierol

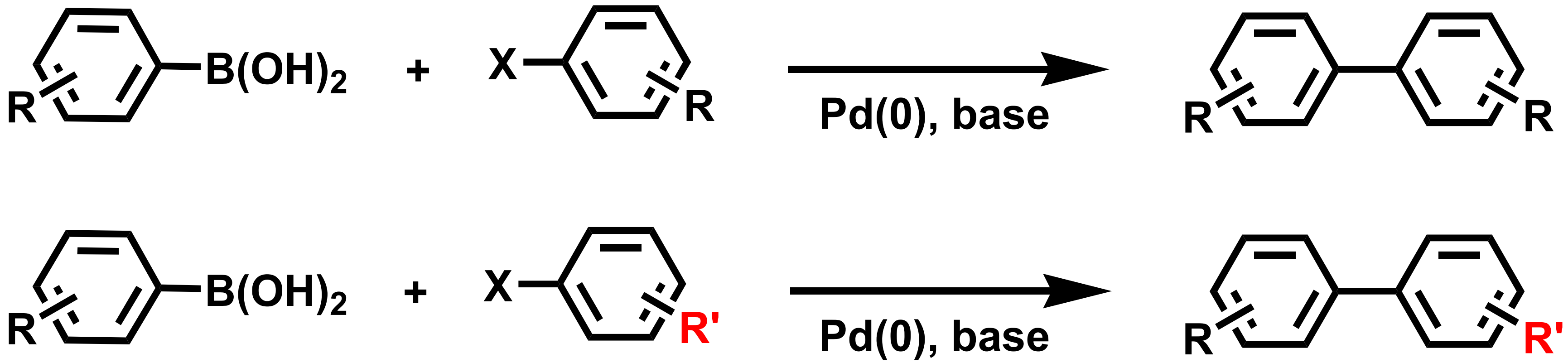


Gymnocin-A

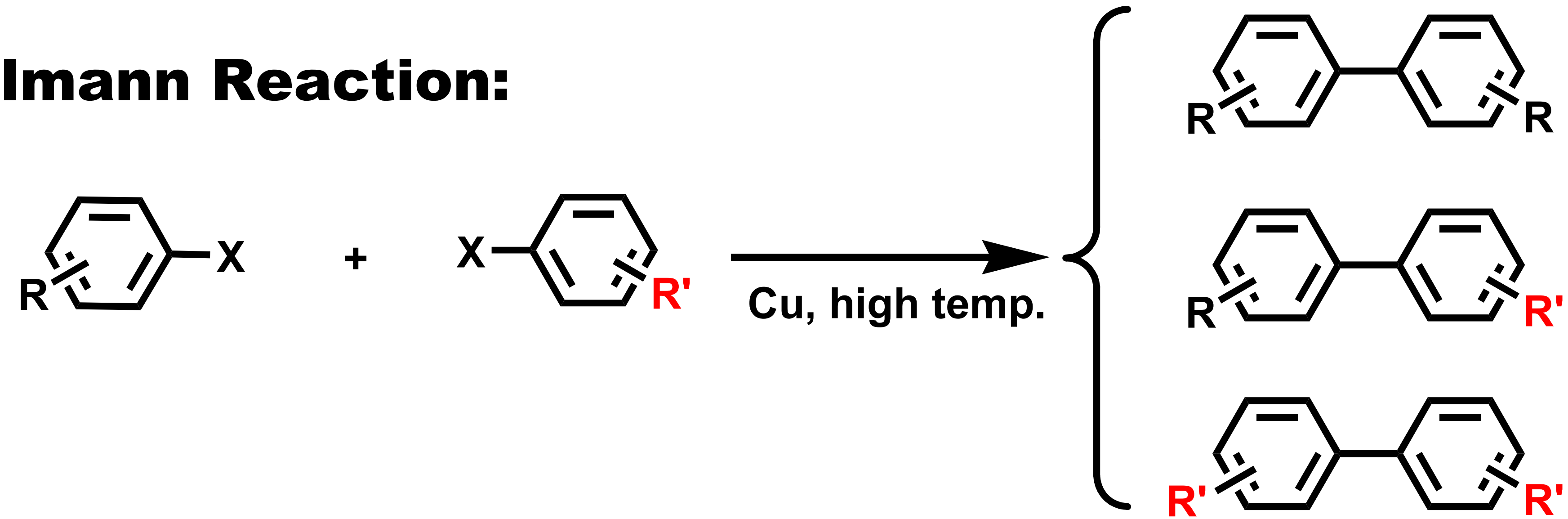
Aromatic-Aromatic Cross-Coupling Reactions



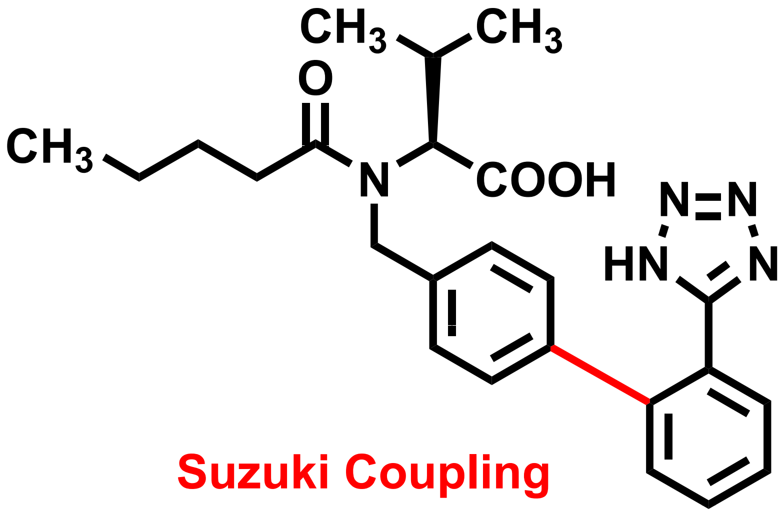
Suzuki Coupling:



Ullmann Reaction:



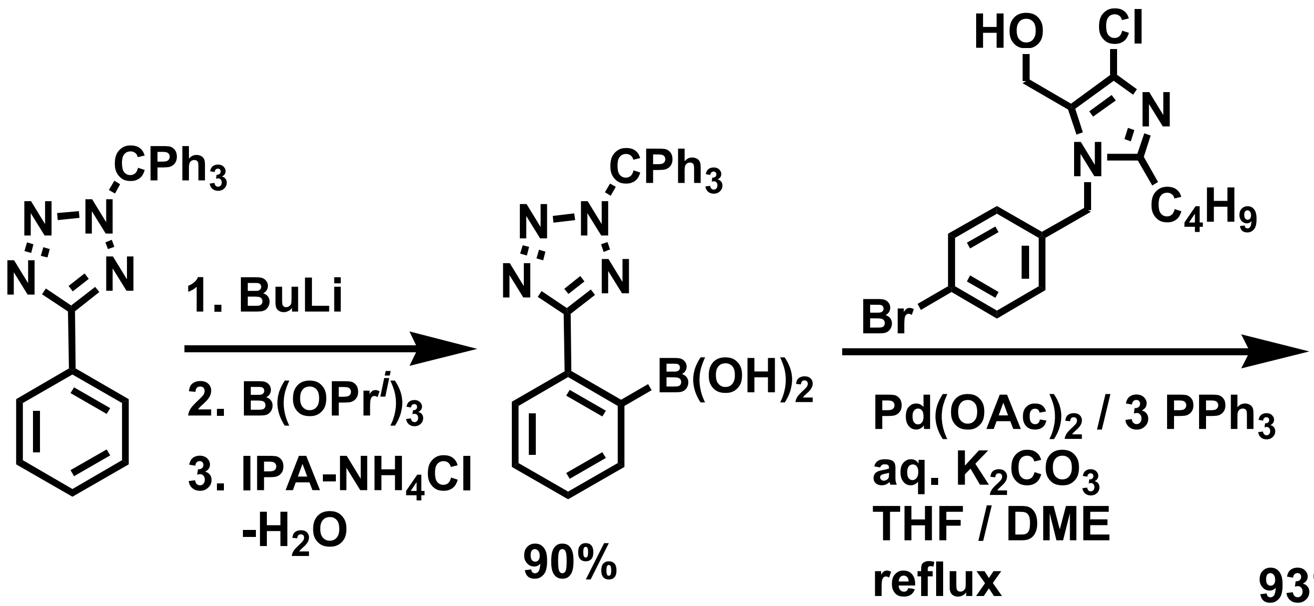
Valsartan (Novartis): Antihypertensive



3.5 million users in Japan

22 million users in the whole world

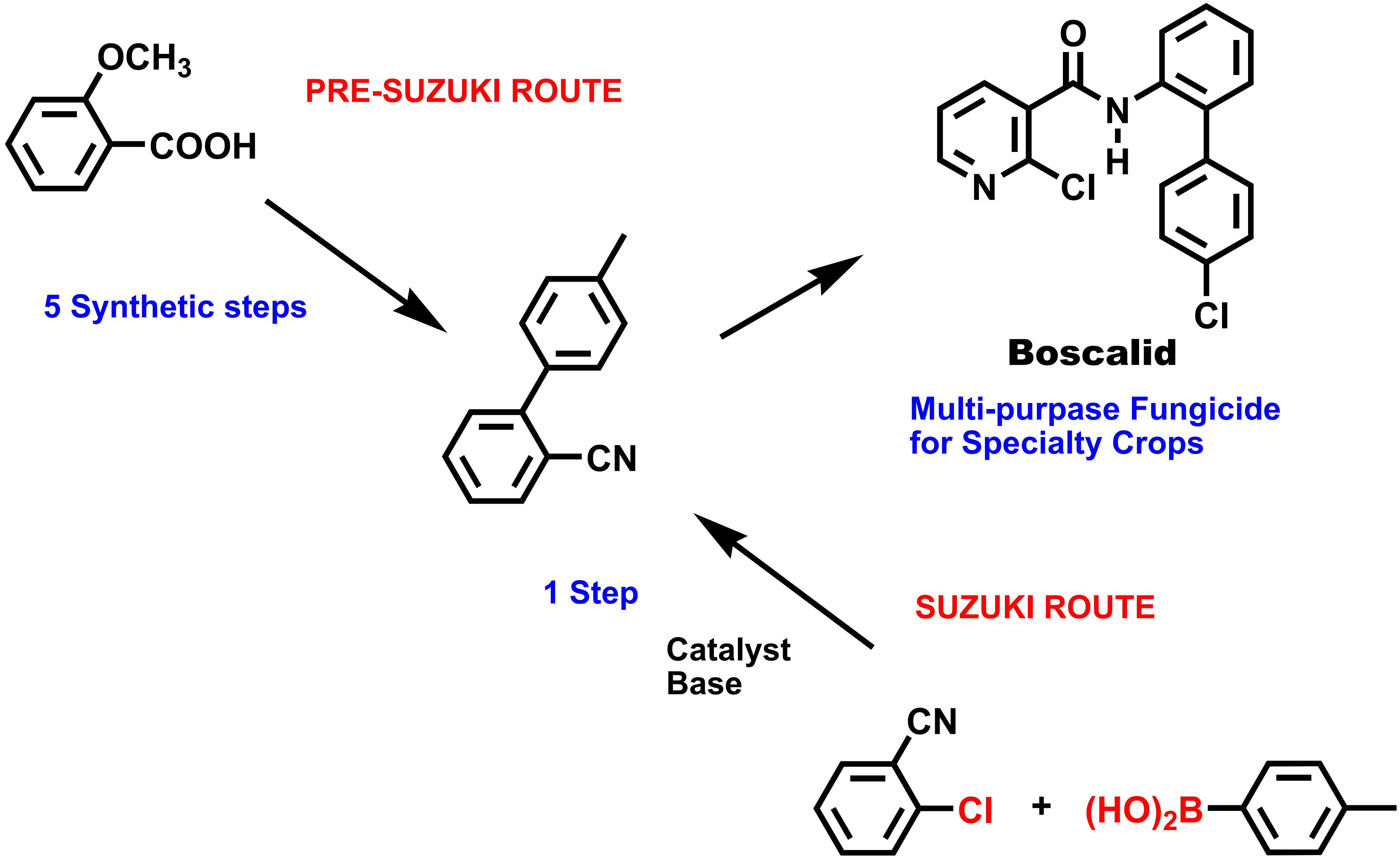
Angiotensin II Receptor Antagonist (Losartan)



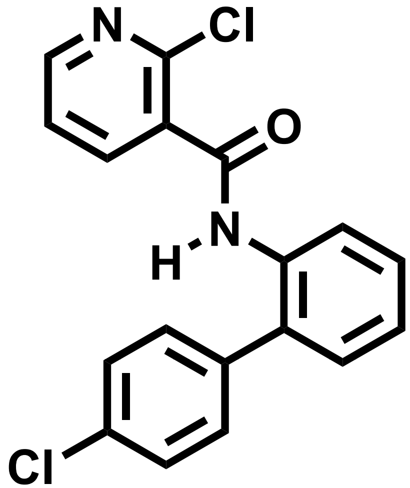
Losartan
(Antihypertensive)

Merck , *J. Org. Chem*. **59**, 6391 (1994)

Suzuki coupling is a shortcut to biaryls (BASF's Boscalid Process)

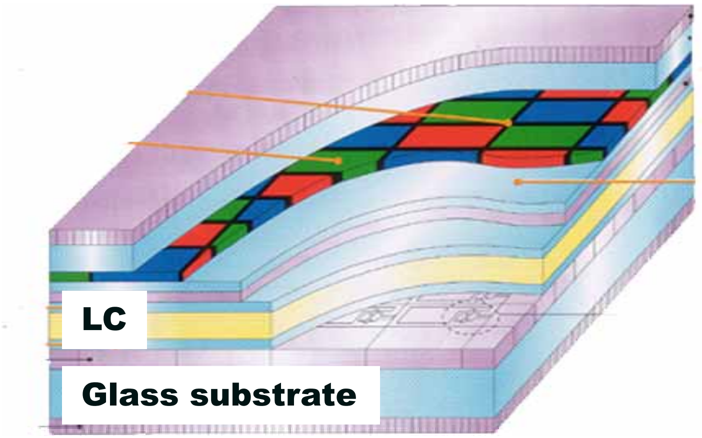


Boscalid; Agrochemicals (BASF, Germany)

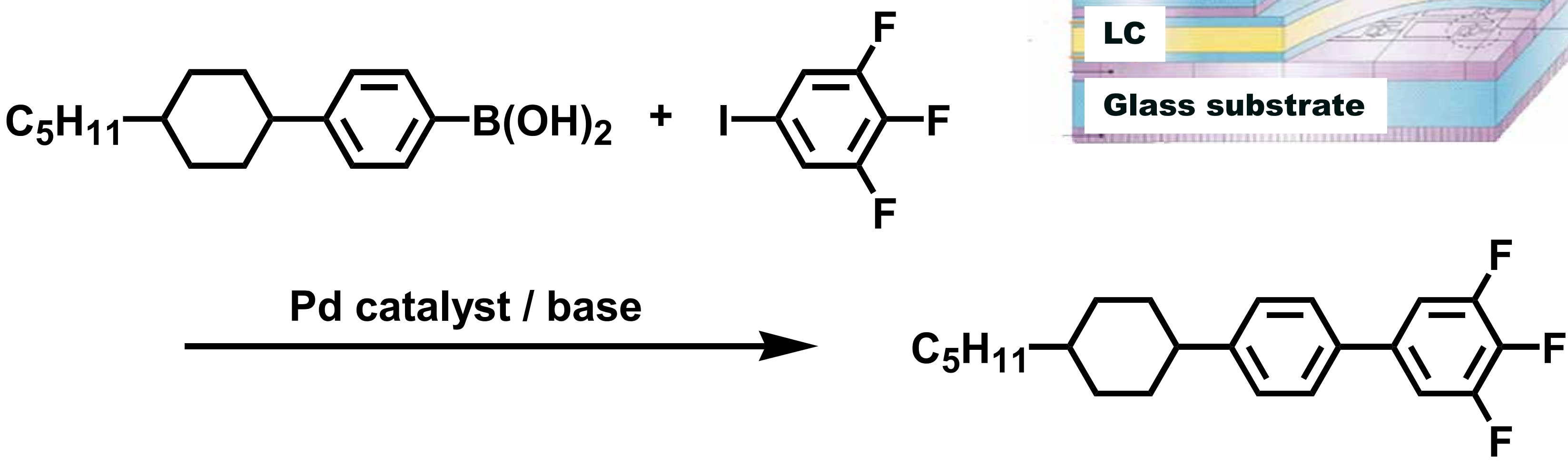


Boscalid

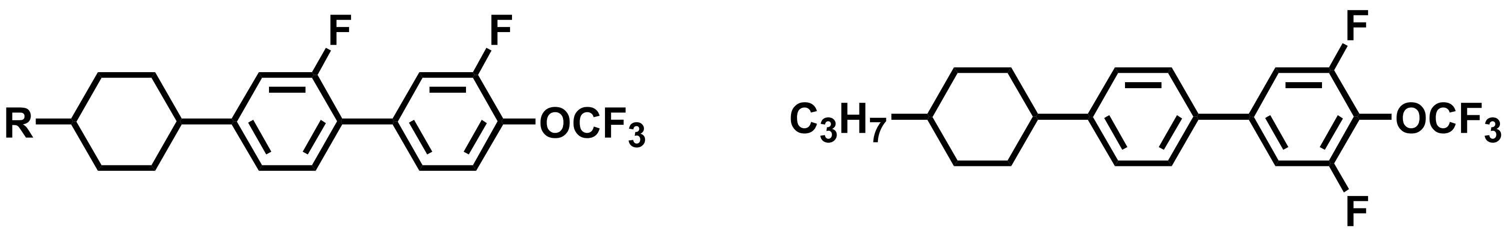
Liquid crystal:



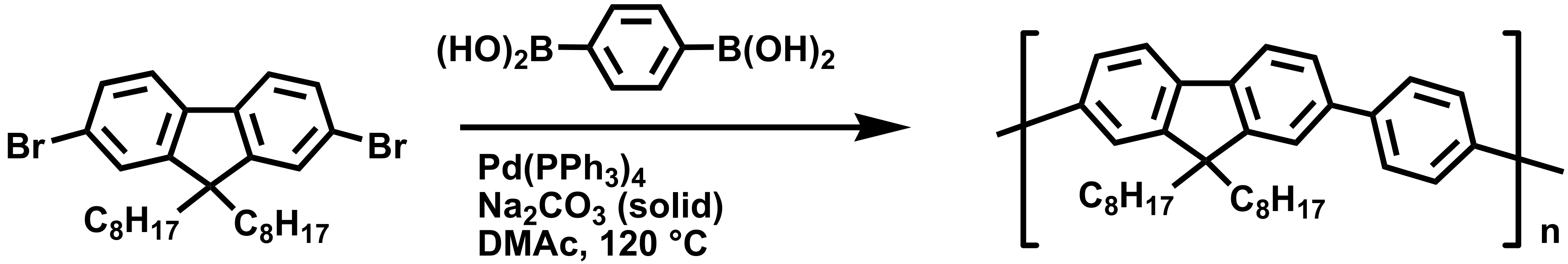
Chisso (Japan)

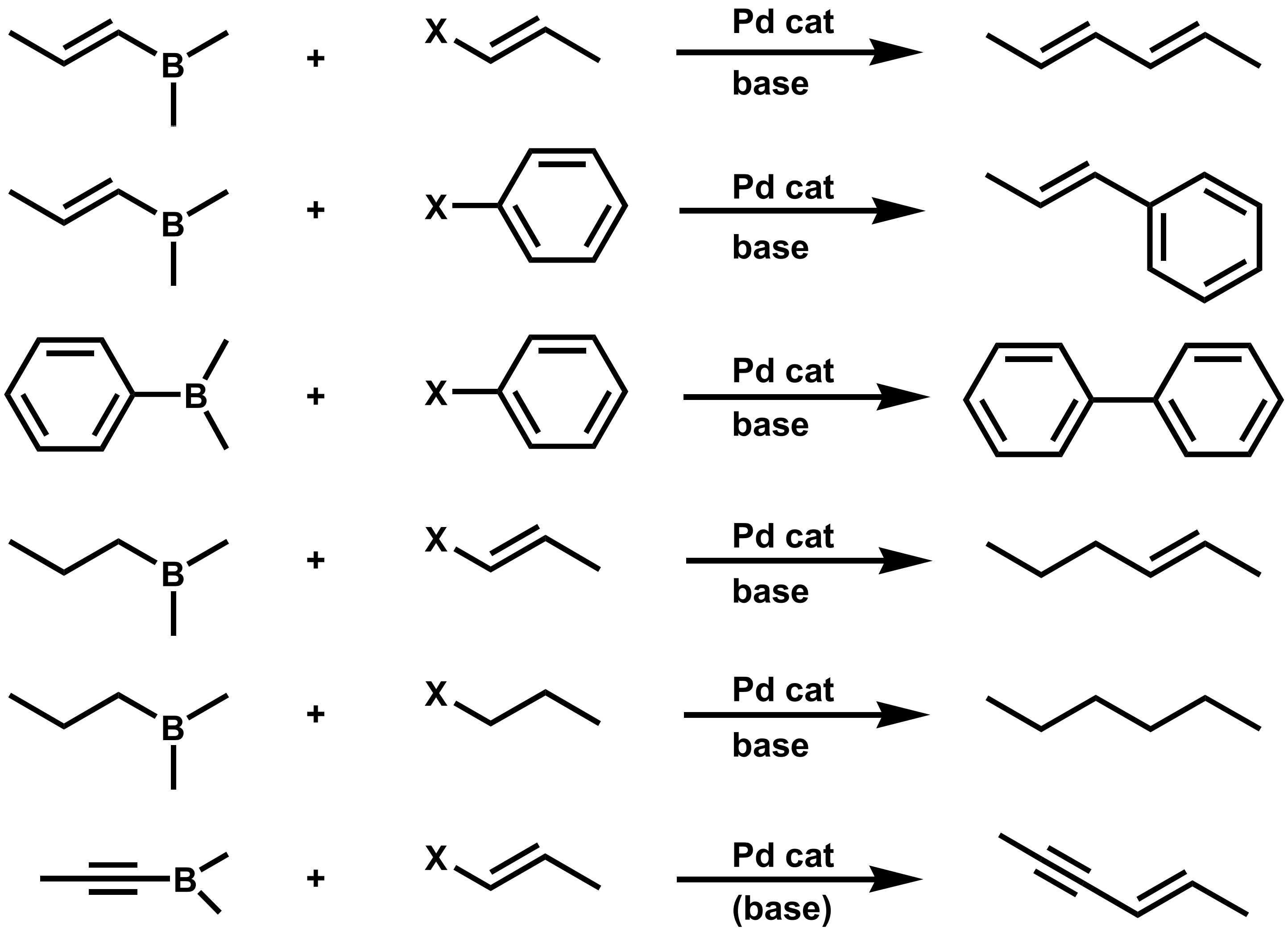


Merck (Germany)



EL Polymer materials





(1979)

(1980)

(1981)

(1985)

(1992)

Fu 2001-2002

Soderquist and Fürstner 1995

Advantages of the Cross-Coupling Reaction between Organoboron Compounds and Organic Electrophiles:

1. Ready availability of reagents: hydroboration and transmetalation
2. Mild reaction conditions: base problem
3. Water stability
4. Easy use of the reaction both in aqueous and heterogeneous conditions
5. Toleration of a broad range of functional groups
6. High regio- and stereoselectivity of the reaction
7. Insignificant effect of the steric hindrance
8. Use of a small amount of catalysts
9. Application in one-pot synthesis
10. Nontoxic reaction
11. Easy separation of inorganic boron compounds