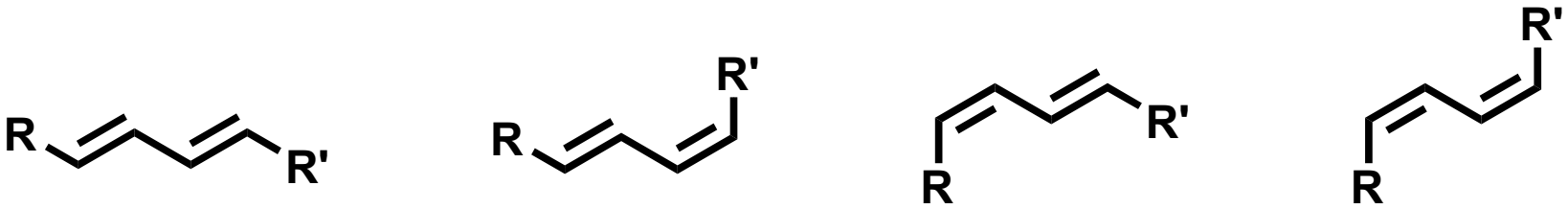
Nobel Lecture, December 8, 2010

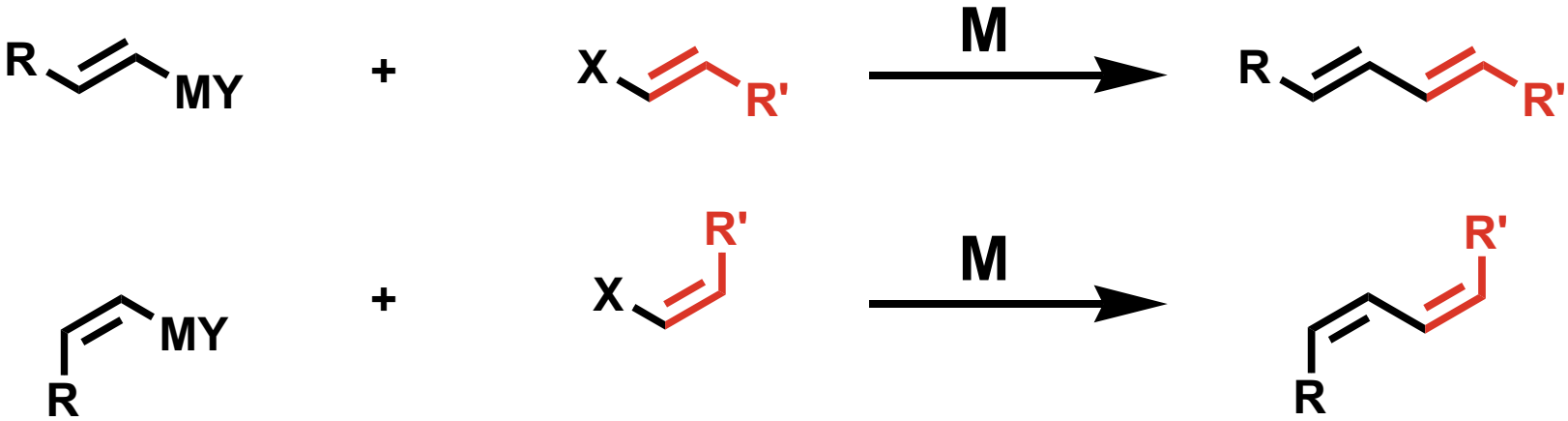
Cross-Coupling Reactions of Organoboranes: An Easy Way for Carbon-Carbon Bonding

Akira Suzuki

Conjugated Alkadienes

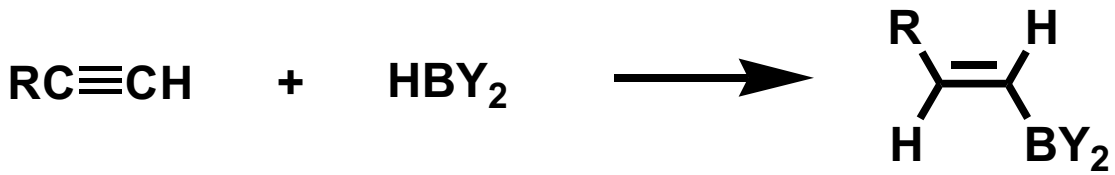


trans-trans　　trans-cis　　cis-trans　　cis-cis



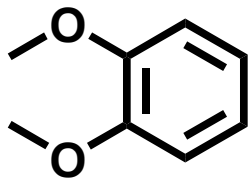
M : transition metal catalyst

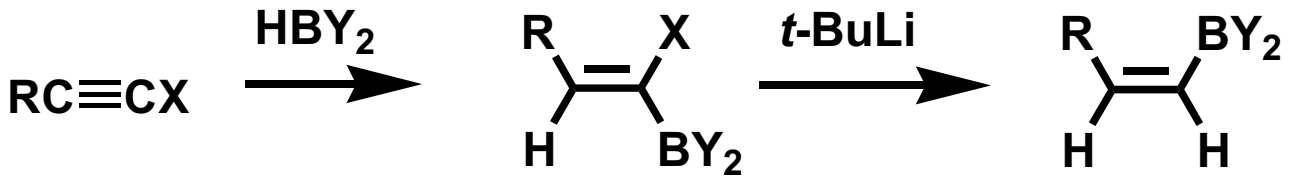
Syntheses of (E)- and (Z)-1-Alkenylboranes



trans > 99 %

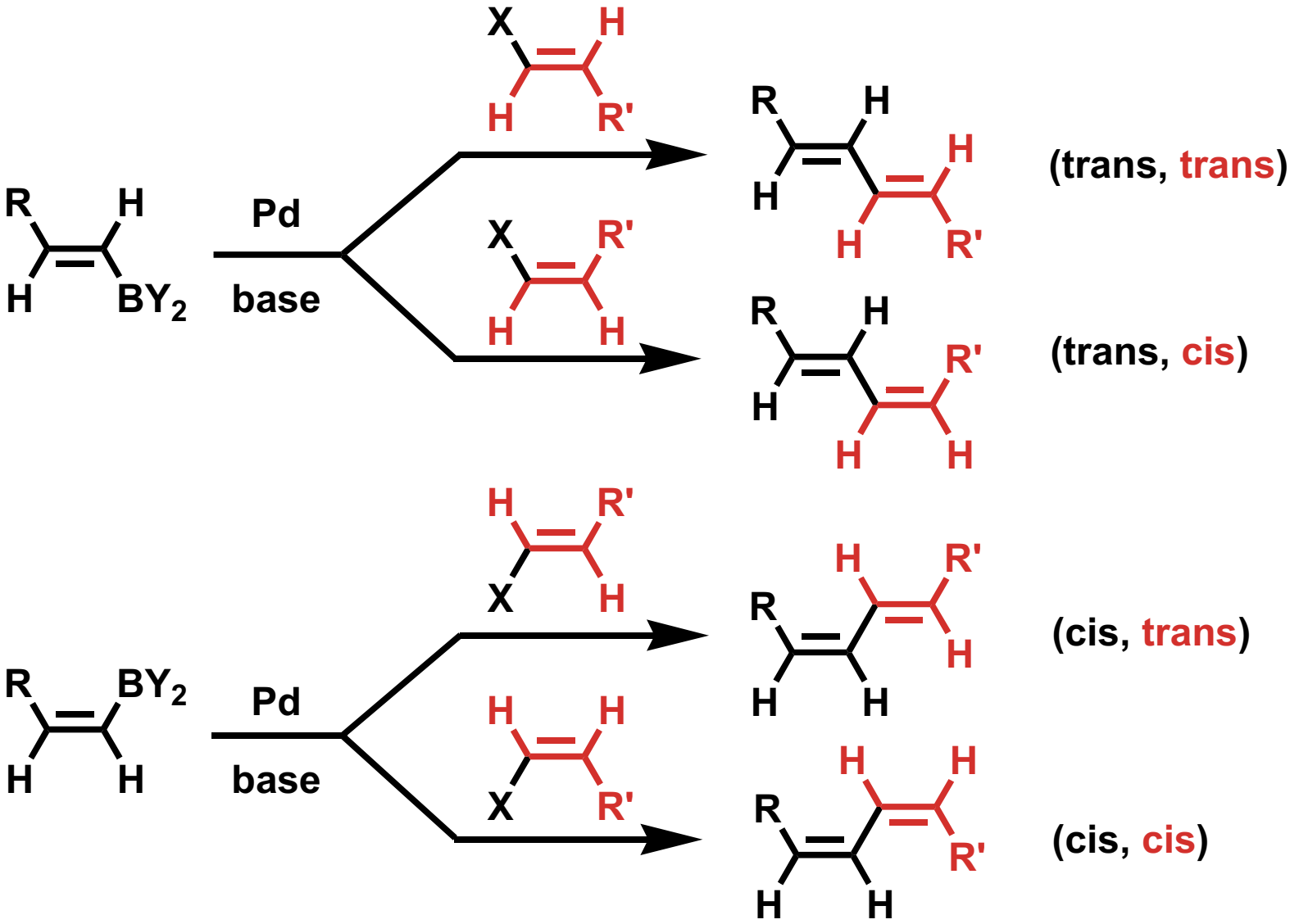
Y_2 = (Siamyl)$_2$,



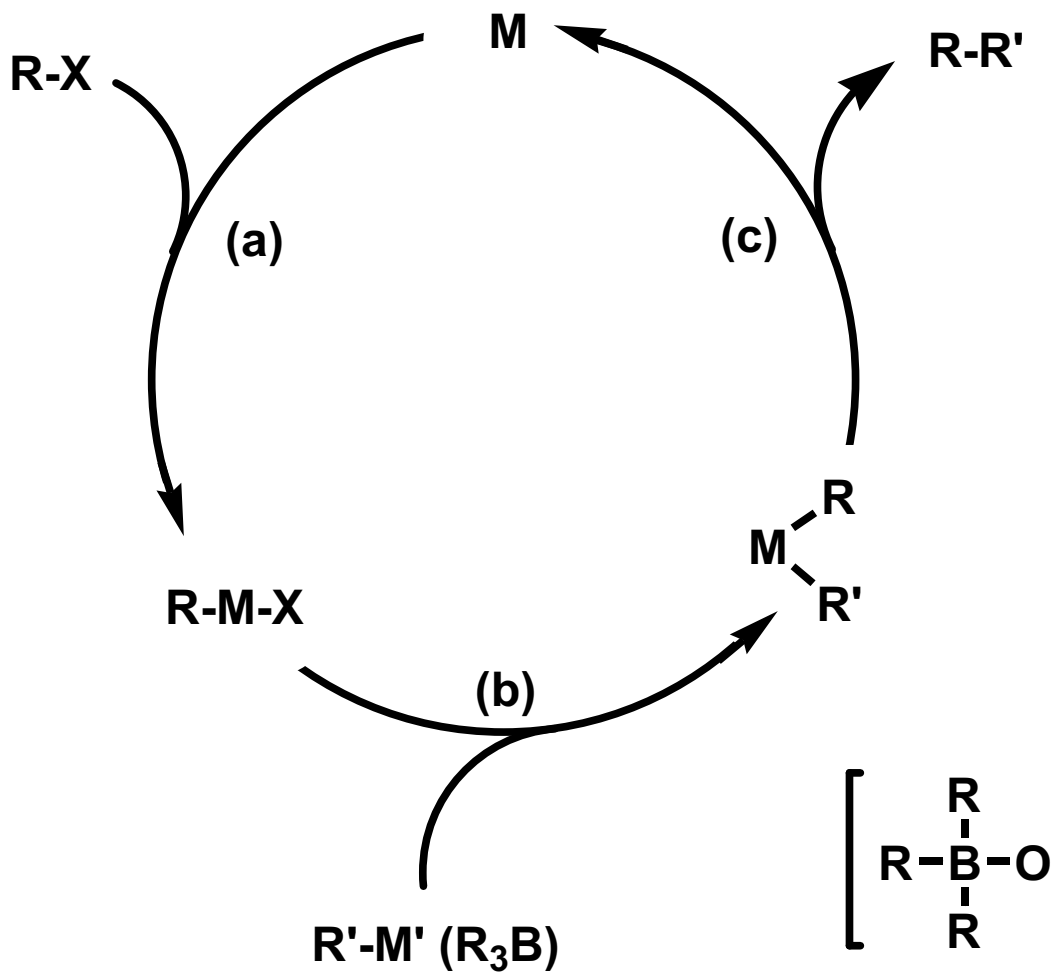


cis > 98 %

X = I or Br Y = Siamyl, Cyclohexyl

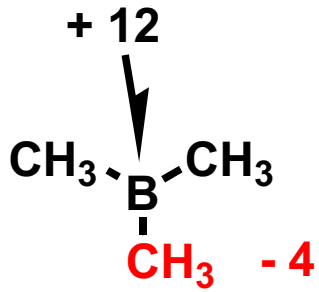

R
H
H
BY2
Pd
base
X
H
H
R'
X
R'
H
H
R
H
H
H
R'
(trans, trans)
R
H
H
R'
H
H
(trans, cis)
H
R'
X
H
H
H
X
R'
R
BY2
H
H
Pd
base
R
H
H
R'
H
(cis, trans)
H
H
X
R'
R
H
H
H
R'
(cis, cis)

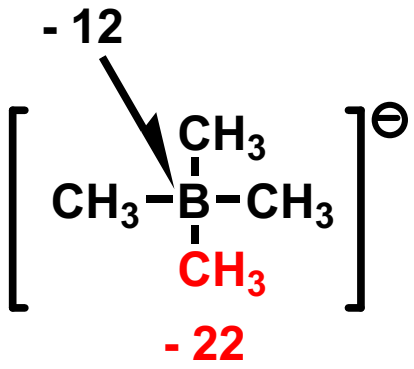
Common Catalytic Cycle Involving Sequential Oxidative Addition (a), Transmetalation (b), and Reductive Elimination (c)

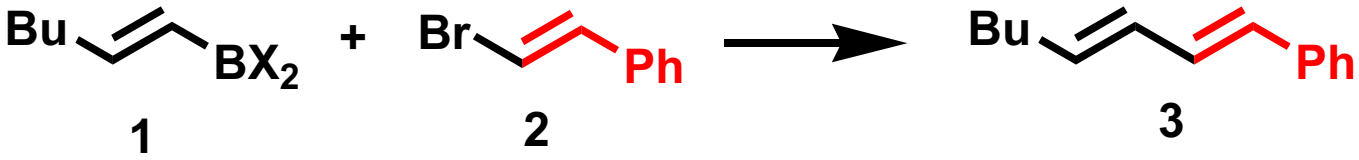


Atomic charge in 0.01 e.u.

(Gropen & Haaland, 1973)

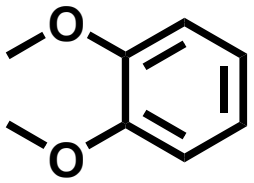


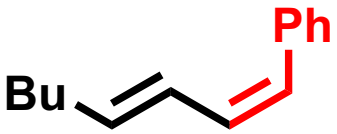
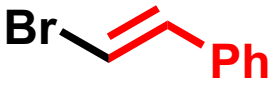
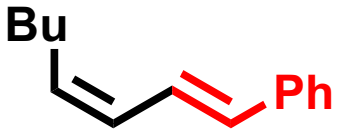
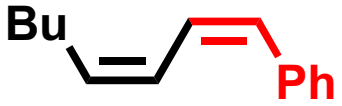
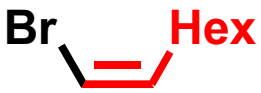
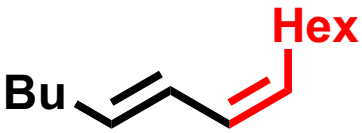
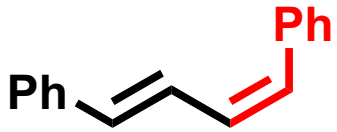




1 2 3

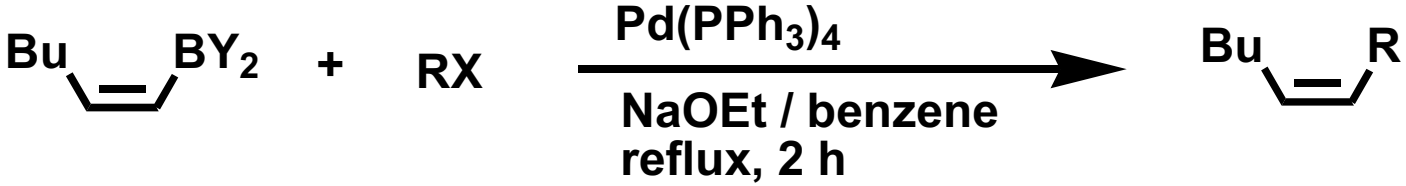
1[a)]	Catalyst[b)] (mol %)	Base (equiv / 2)	Solvent	React. time (h)	Yield (%) of 3
1b	PdL_4 (3)	None	THF	6	0
1b	PdL_4 (3)	None	Benzene	6	0
1a	PdL_4 (3)	2M NaOEt (2)-EtOH	THF	2	73
1b	PdL_4 (3)	2M NaOEt (2)-EtOH	THF	4	78
1b	PdL_4 (1)	2M NaOEt (2)-EtOH	Benzene	2	86

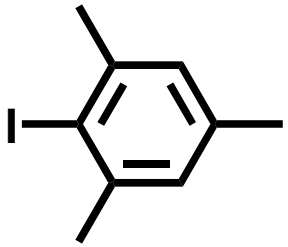
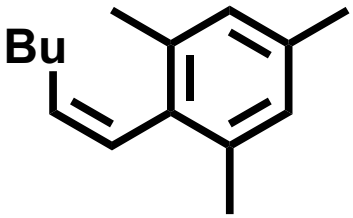
a) 1a, $X_2 = (Sia)_2$ 1b, X_2 =  b) $L = PPh_3$

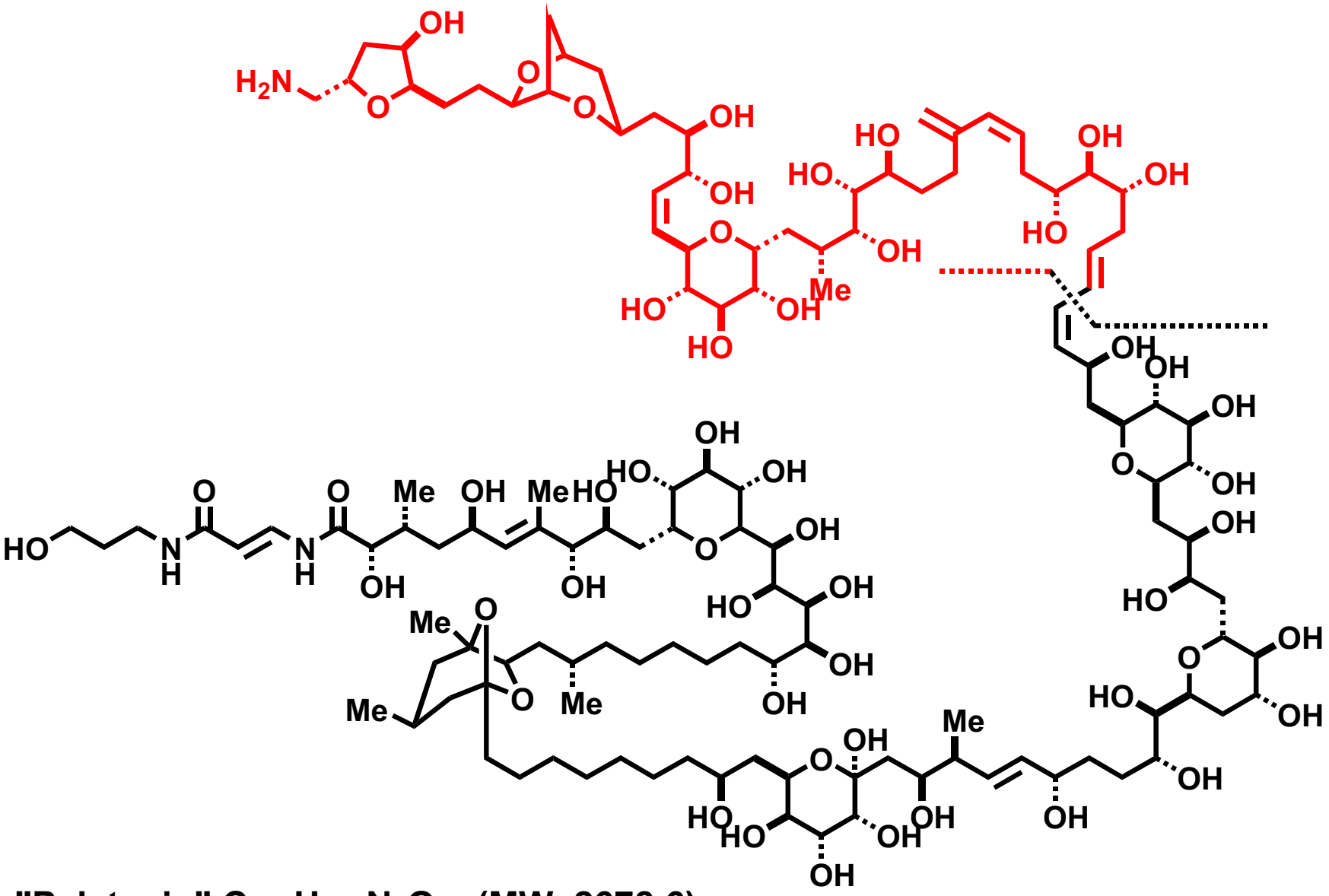
1-Alkenylborane	1-Alkenyl Bromide	Product	Yield (%) [Purity (%)]
 b)			86 [98]
 a)			49 [99]
 a)			42 [89]
 b)			88 [99]
 a)			49 [98]
 b)			89 [98]

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

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



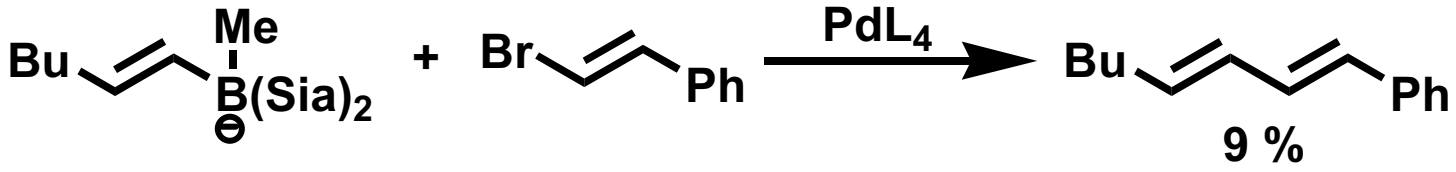
BY_2	RX	Product	Yield (%)	Purity (%)
$B(Sia)_2$			49	>98
$B(OPr^i)_2$			87	>99
$B(Sia)_2$			58	>94
	PhI		49	>83
$B(OPr^i)_2$			98	>97
$B(Sia)_2$			54	>92
$B(OPr^i)_2$			87	>99

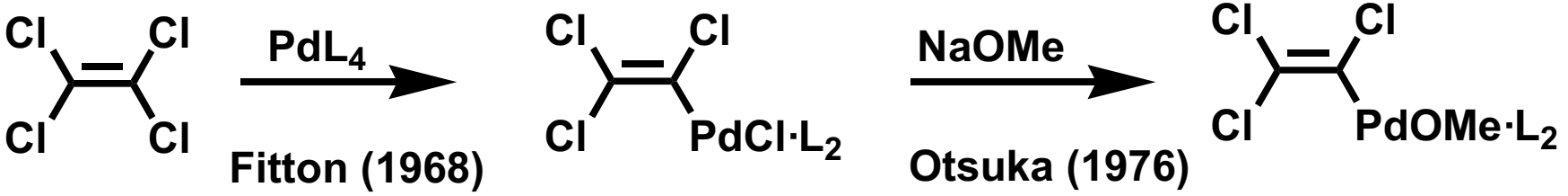


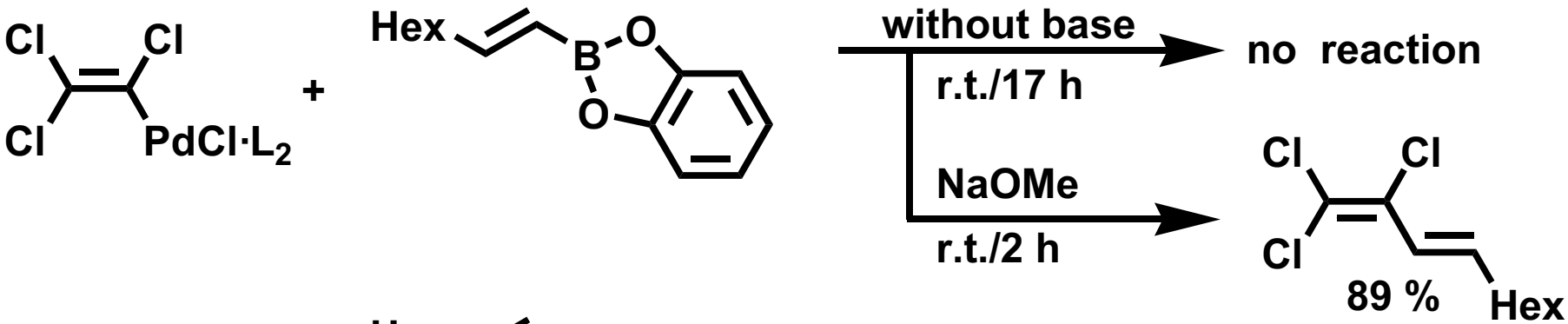
"Palytoxin" $C_{129}H_{223}N_3O_{54}$ (MW. 2678.6)

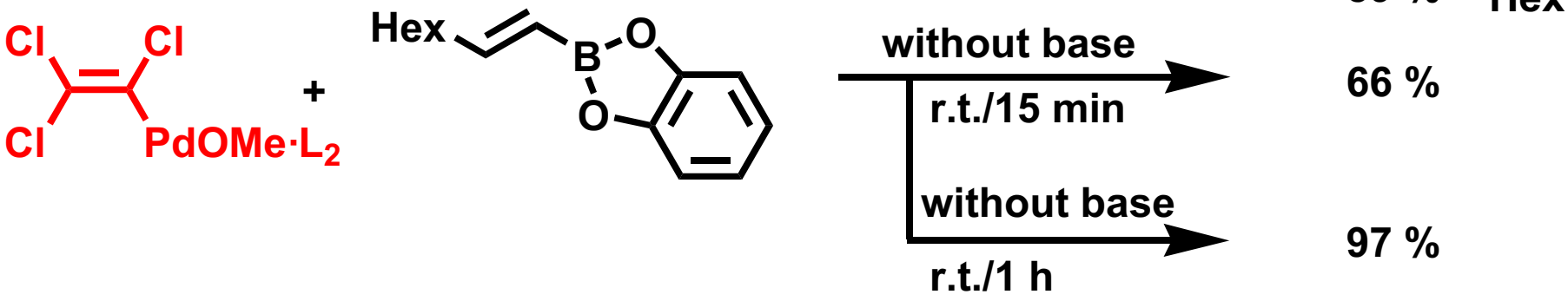
Synthesis: Kishi et al., *J. Am. Chem. Soc*, 1989, *111*, 7525, 7530

Reaction Mechanism:

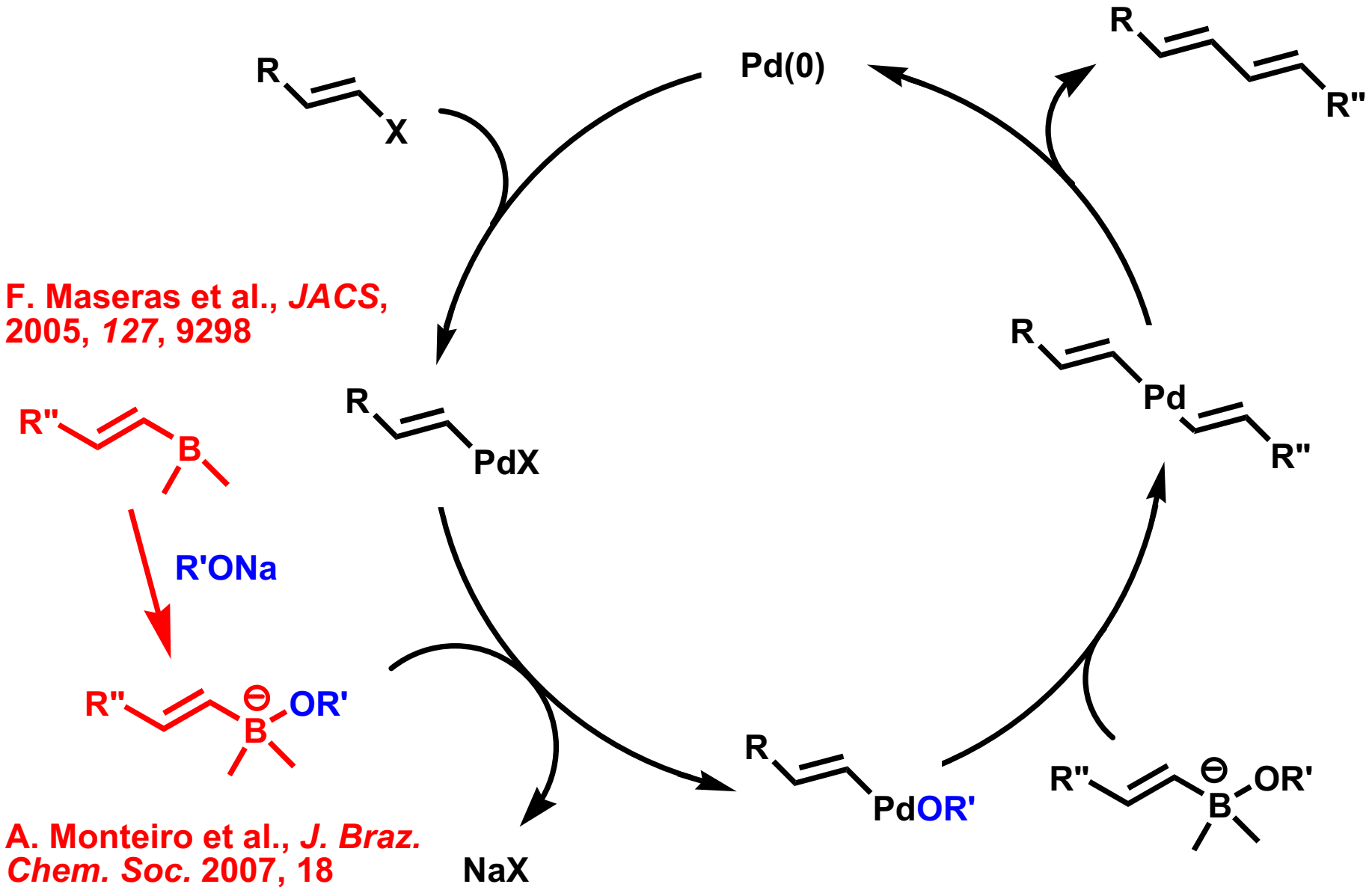




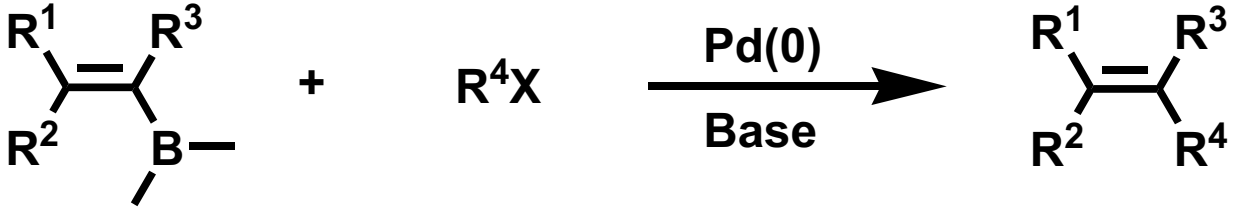




Catalytic Formulation of the Vinyl-Vinyl Cross-Coupling

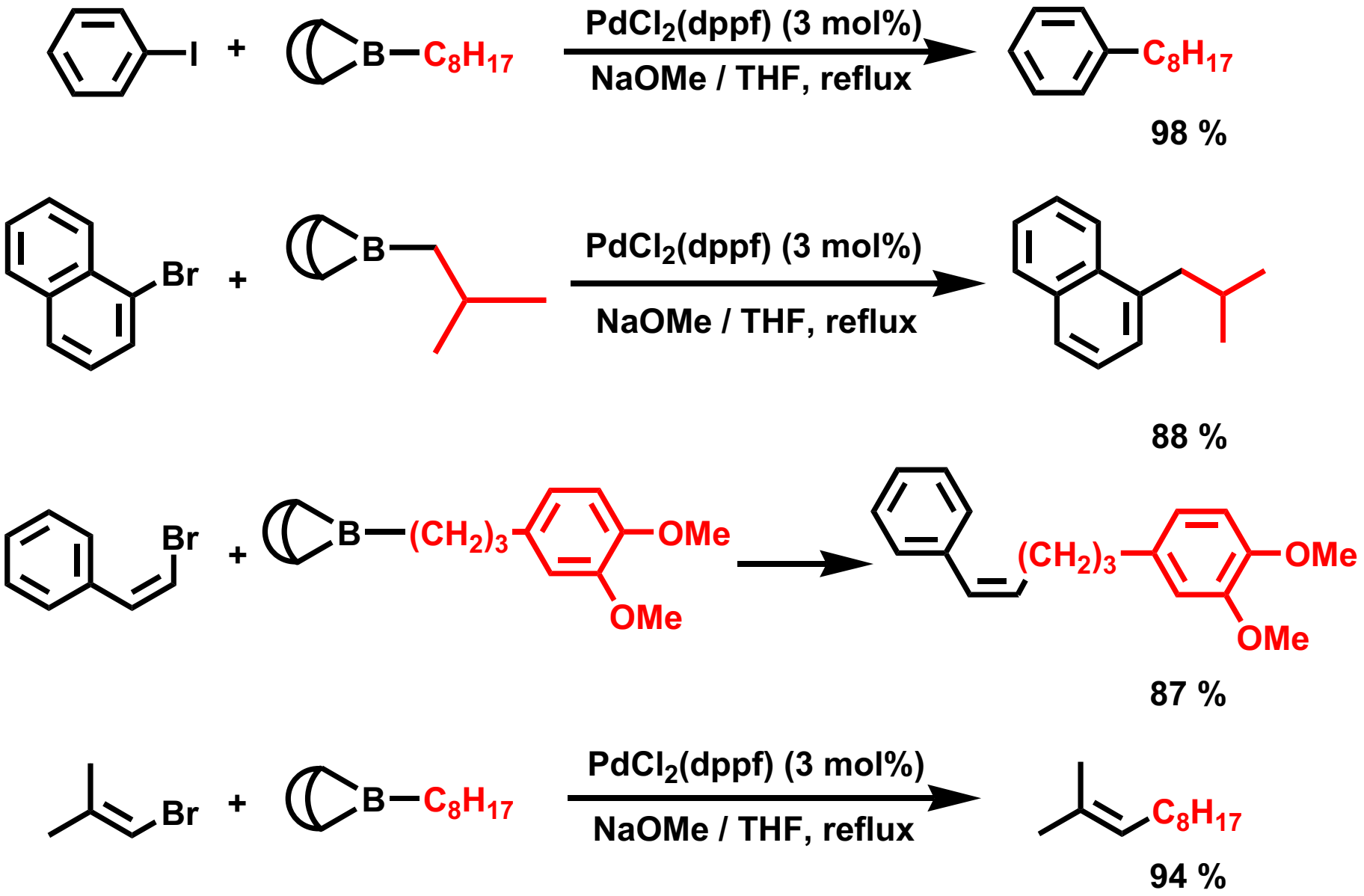


Reaction of B-Alkylboranes



R4 : 1-Alkenyl
Aryl
1-Alkynyl
Allyl
Benzyl

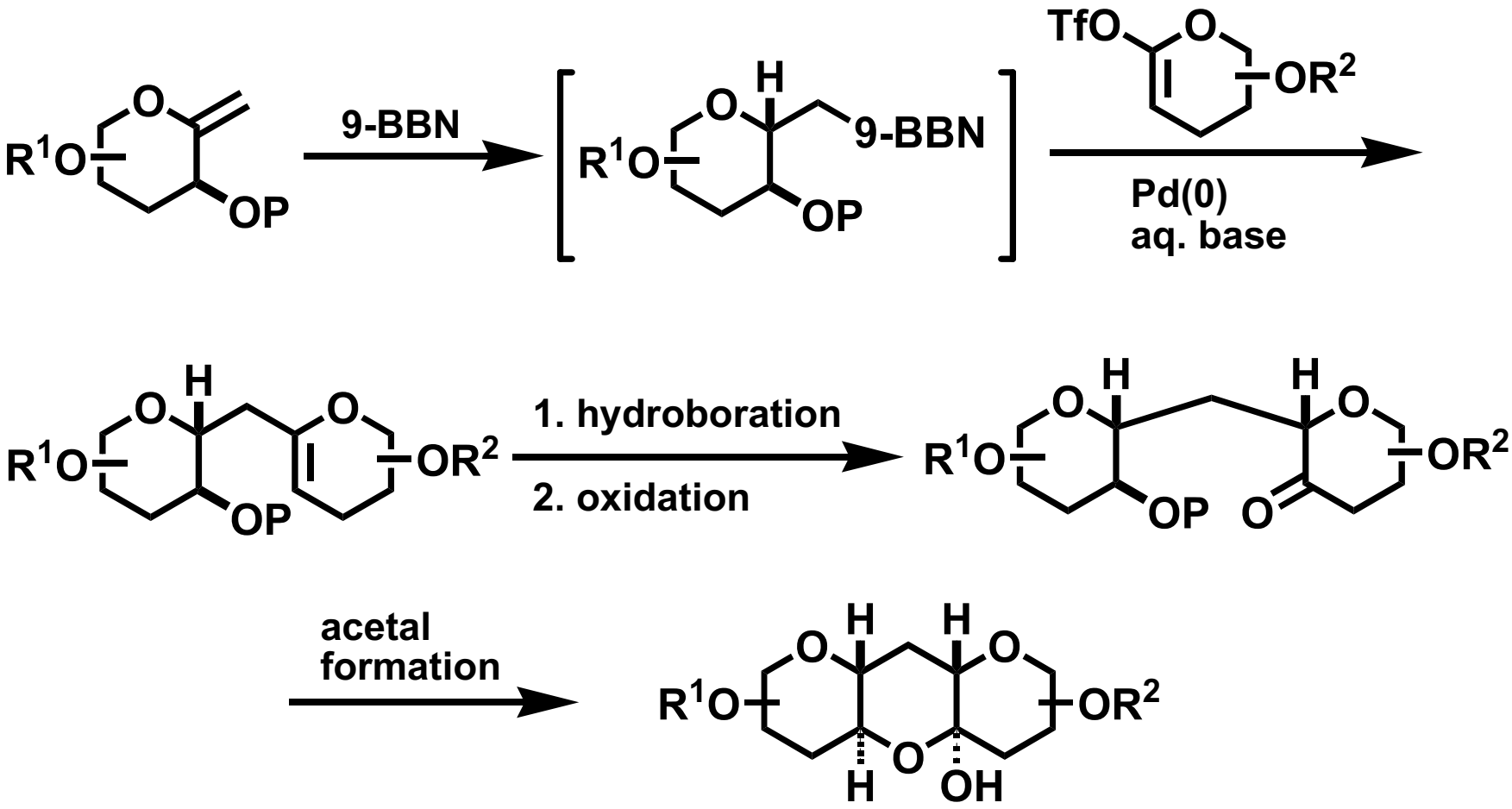
R : Alkyl


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

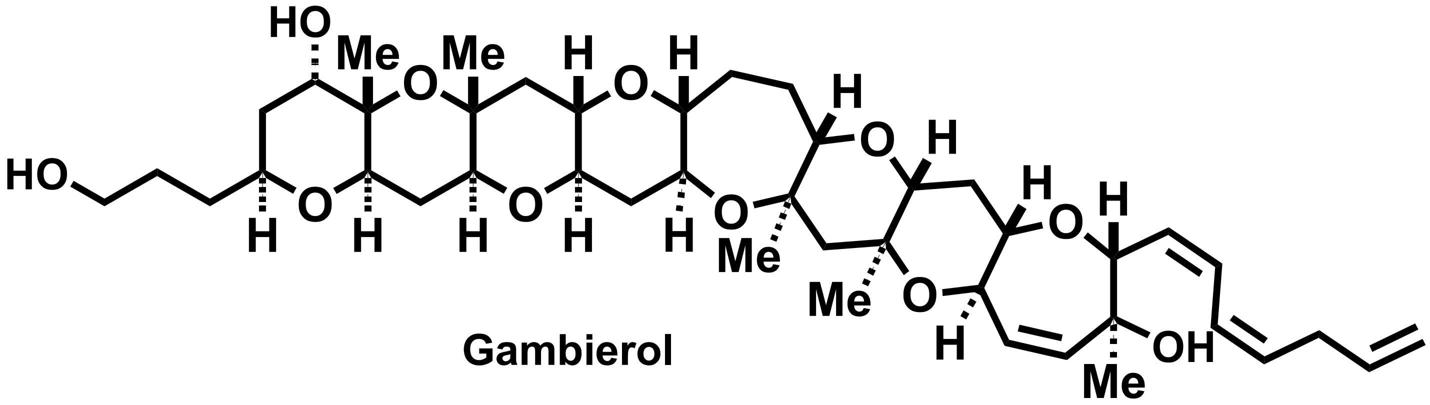
Alkyl-Vinyl Coupling:

Total Synthesis of Polycyclic Ether Natural Product

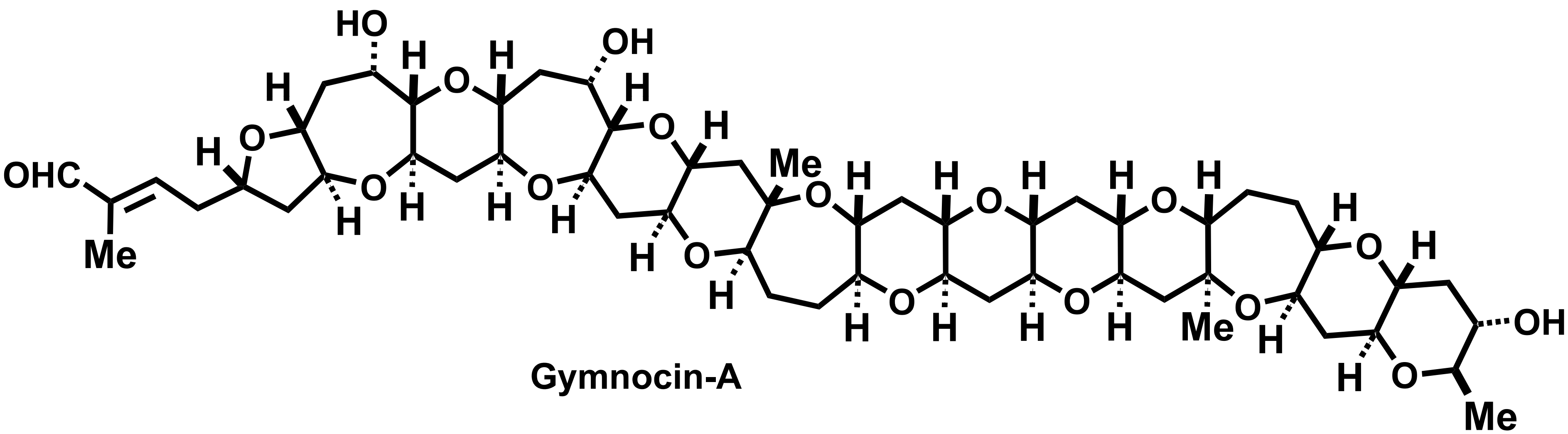
M. Sasaki, *Bull. Chem. Soc. Jpn.* 2007, *80*, 856



Polycyclic Ether Marine Natural Products:

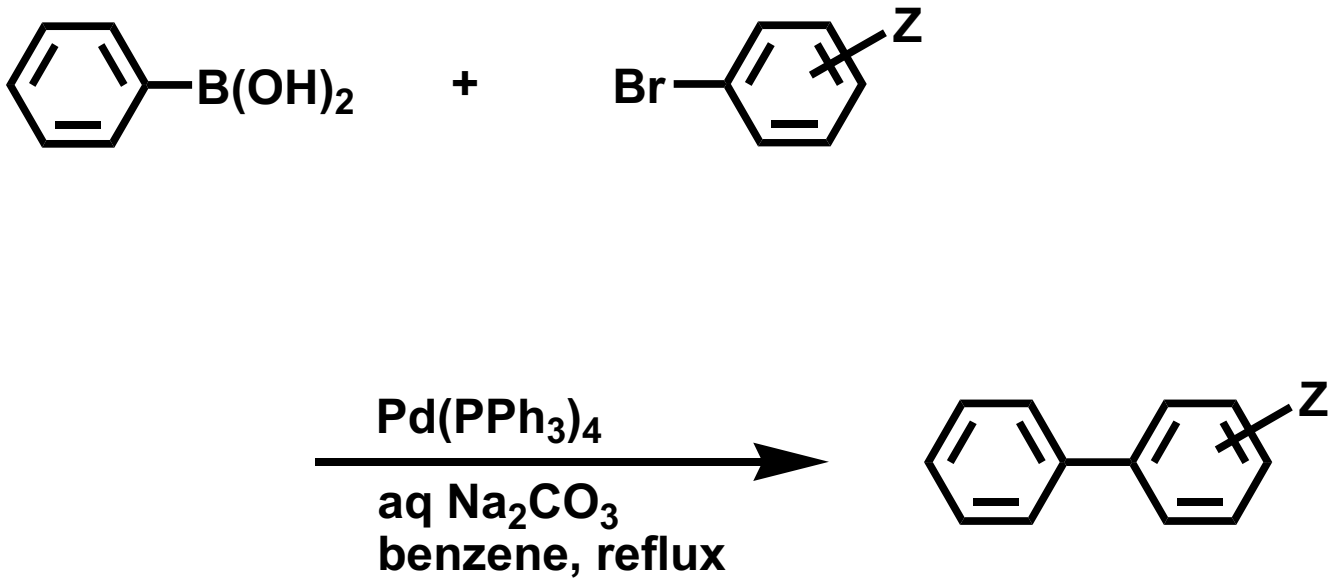


Gambierol

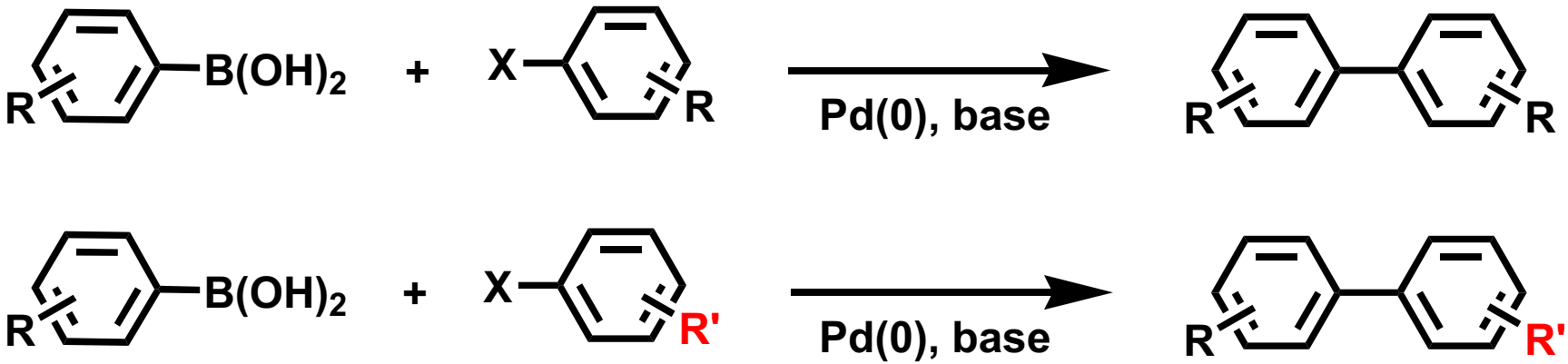


Gymnocin-A

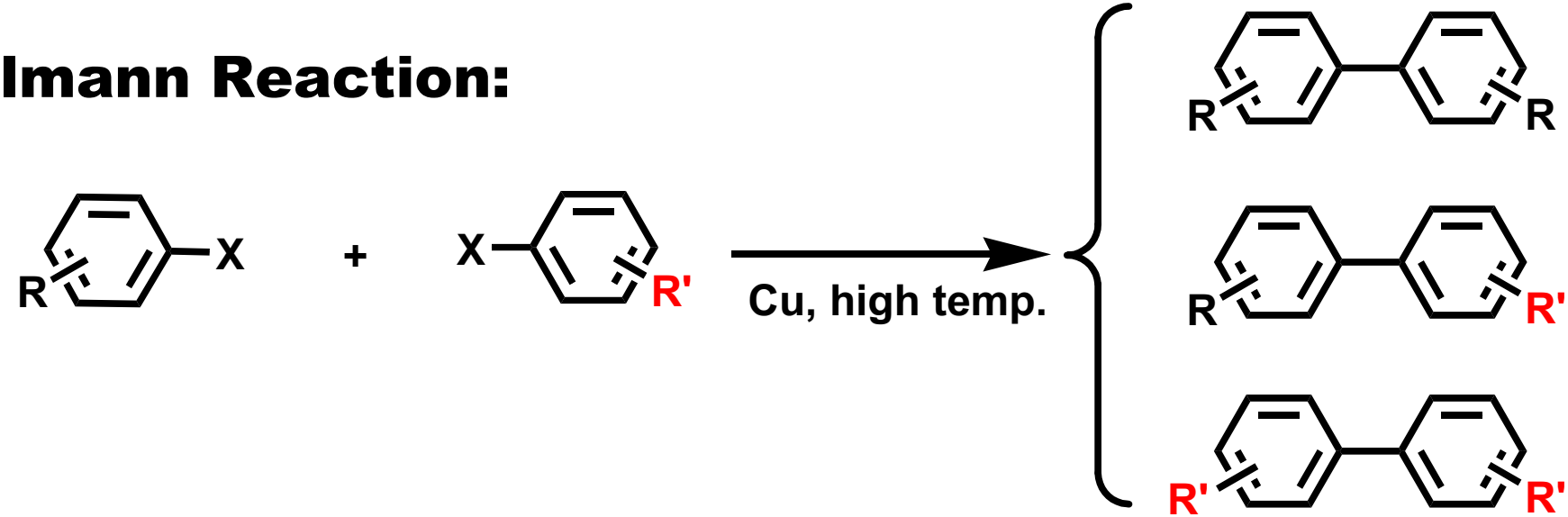
Aromatic-Aromatic Cross-Coupling Reactions



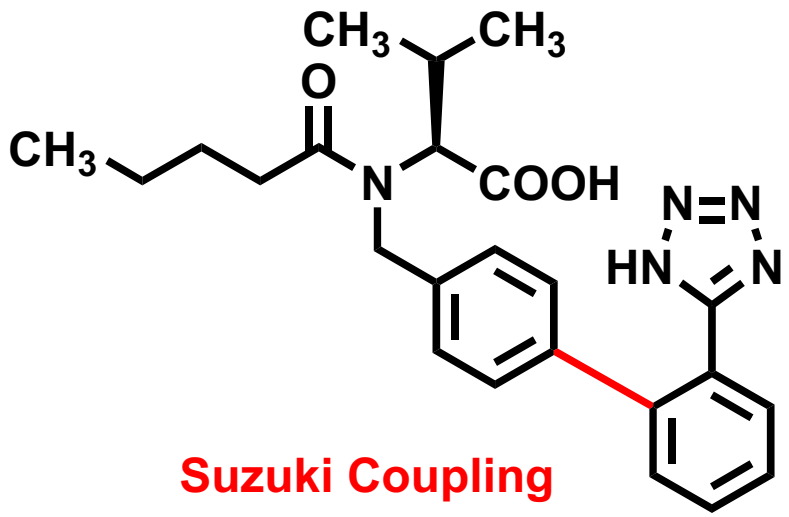
Suzuki Coupling:



Ullmann Reaction:



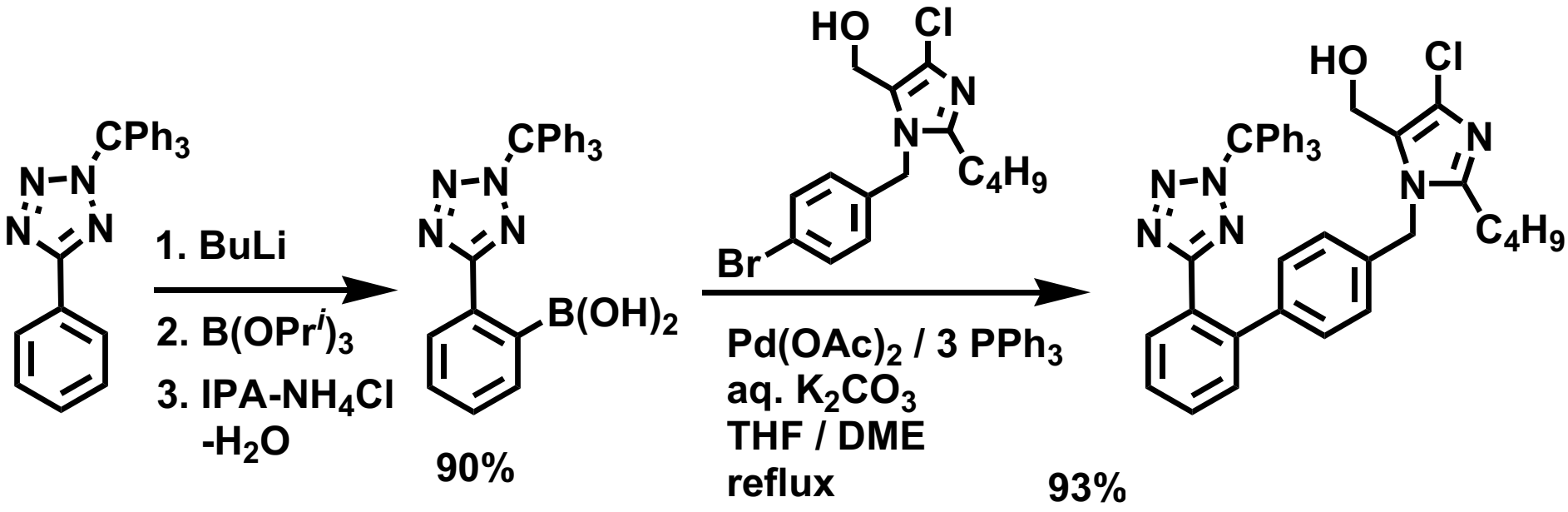
Valsartan (Novartis): Antihypertensive



3.5 million users in Japan

22 million users in the whole world

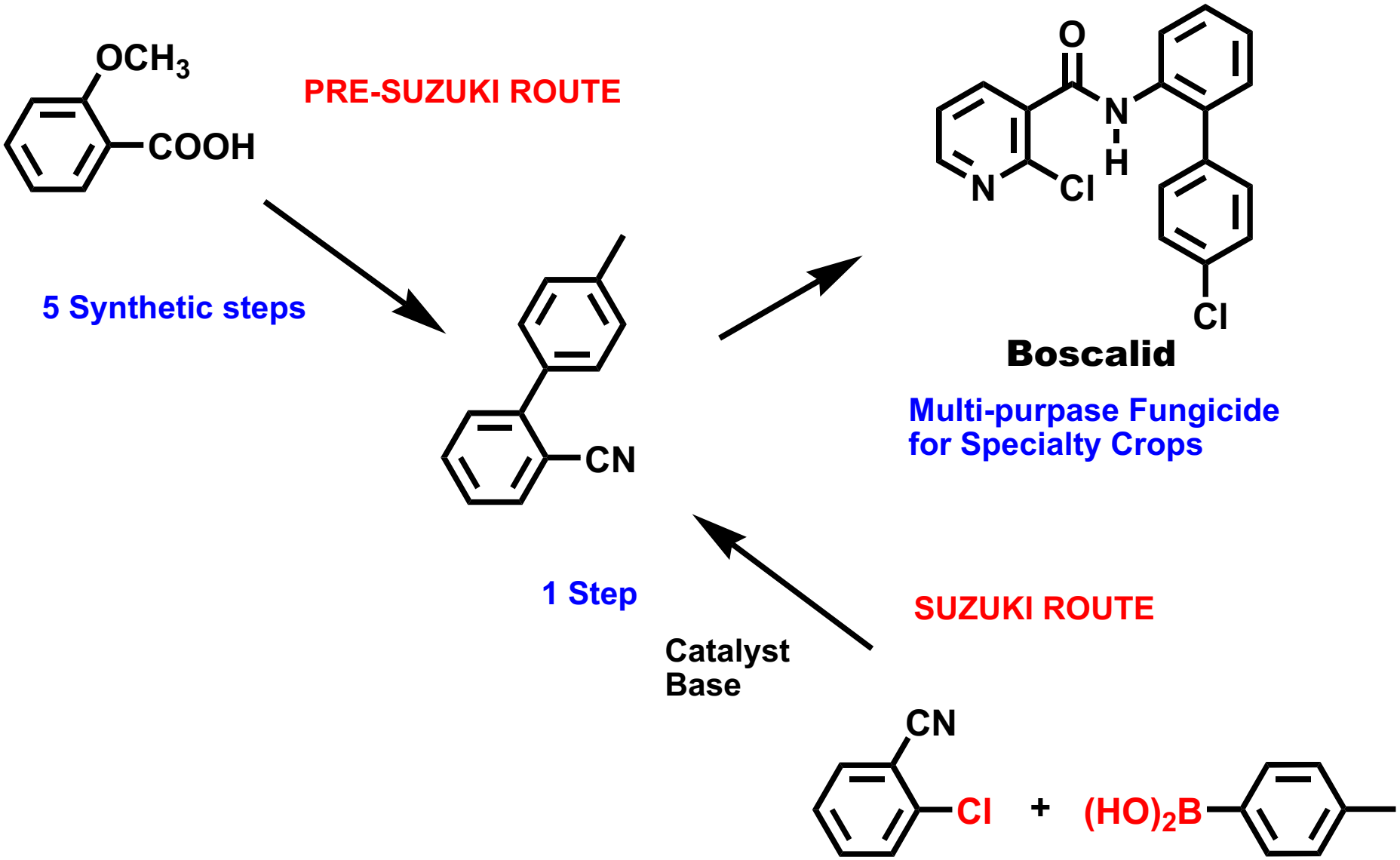
Angiotensin II Receptor Antagonist (Losartan)



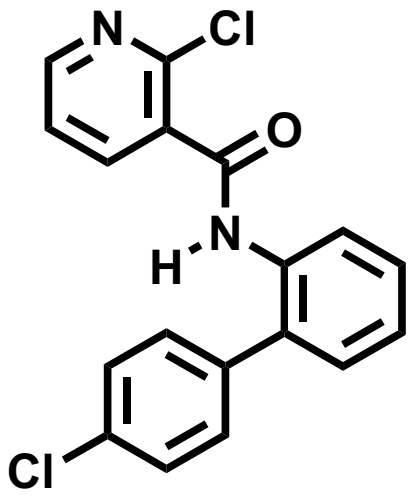
Losartan (Antihypertensive)

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

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

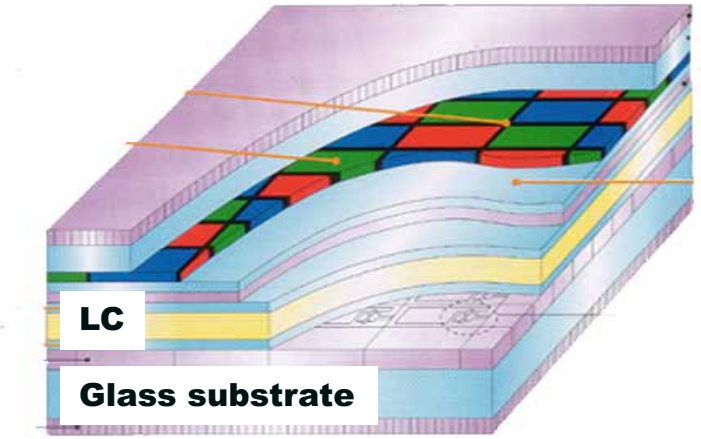


Boscalid; Agrochemicals (BASF, Germany)

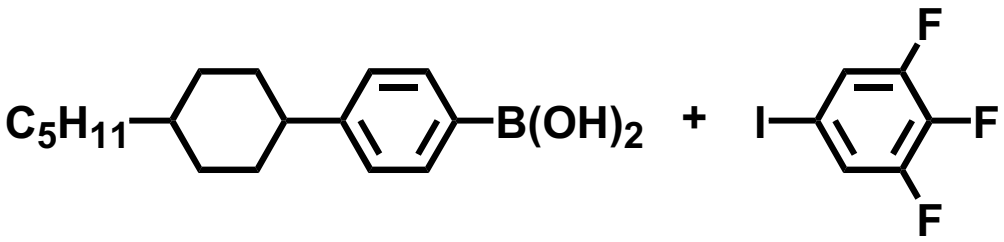


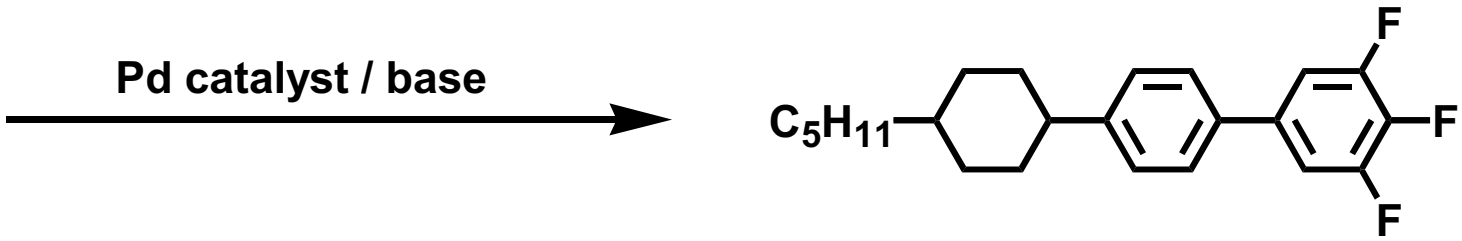
Boscalid

Liquid crystal:

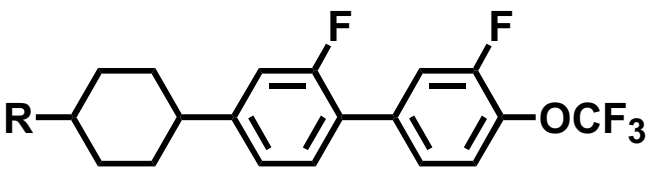


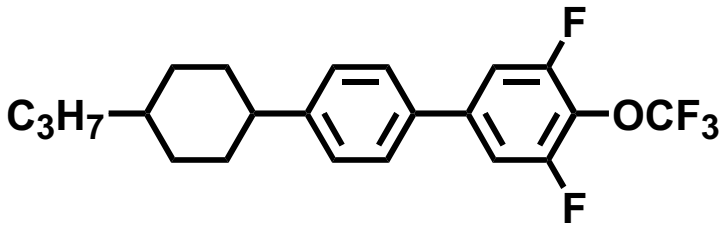
Chisso (Japan)



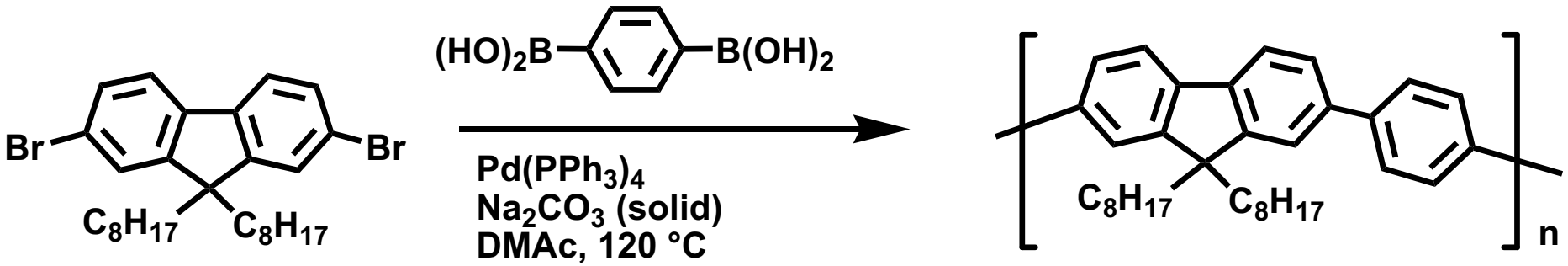


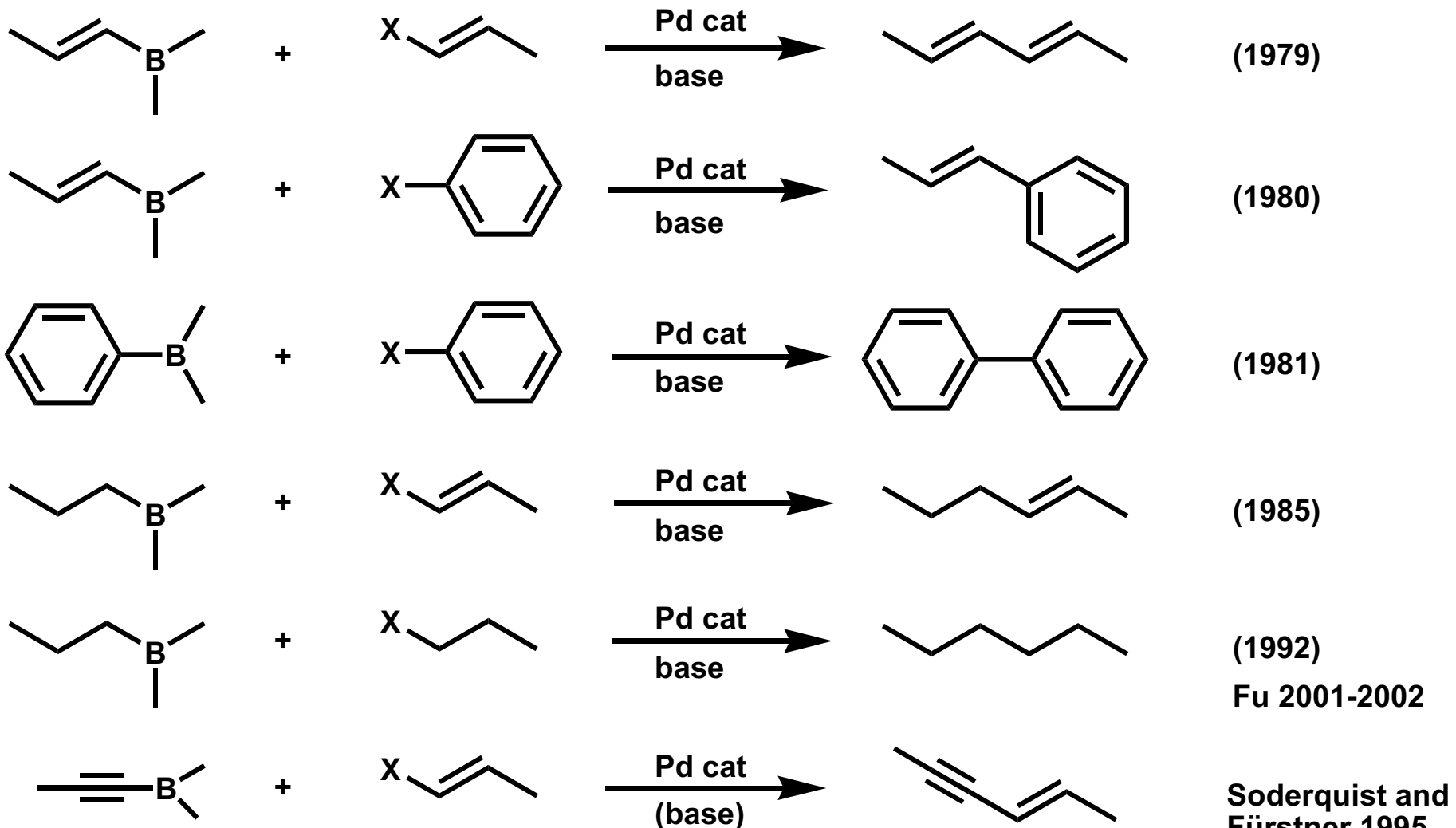
Merck (Germany)





EL Polymer materials




B
+
X
Pd cat
base
(1979)
(1980)
(1981)
(1985)
(1992)
Fu 2001-2002
(base)
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