C-C Cross-Couplings

Kumada

Negishi

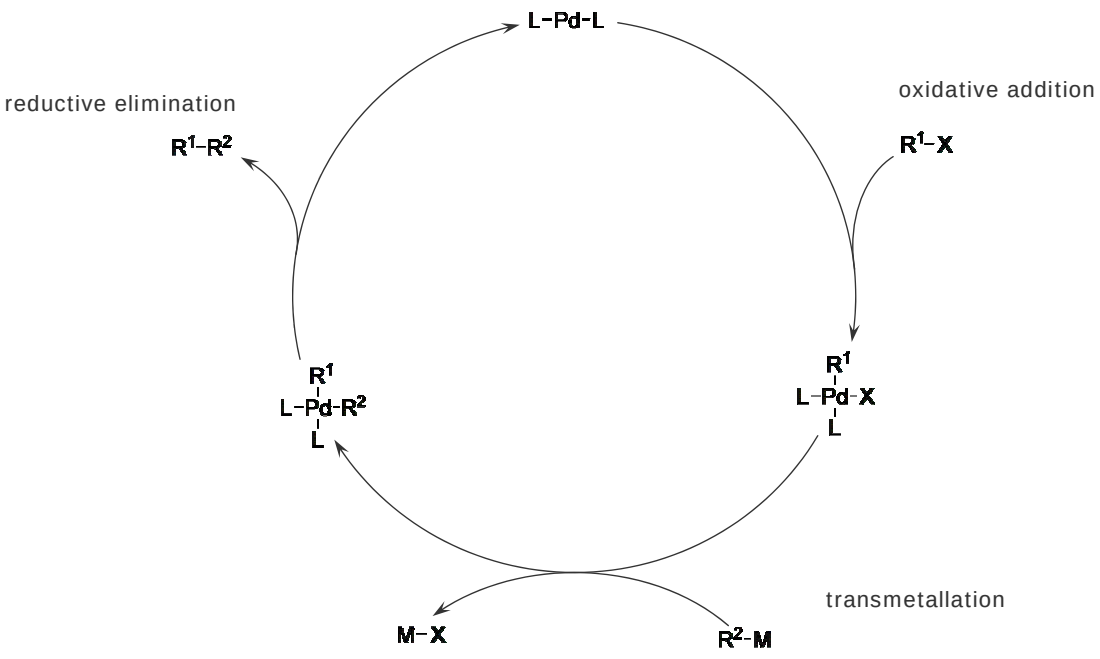
Stille

Suzuki

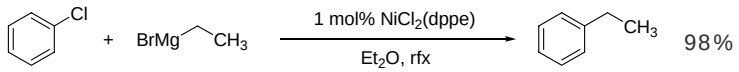
Hiyama

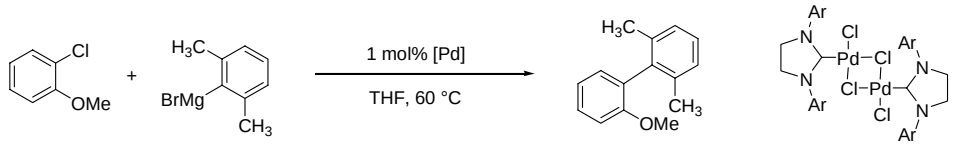
Sonogashira

C-C cross-coupling: Mechanism

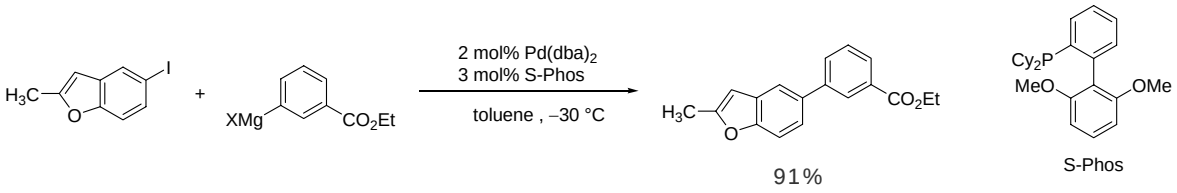


Kumada Coupling





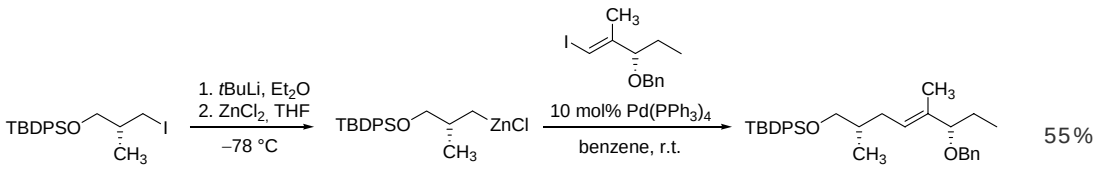
Nolan *JACS* **1999** *121* 9889
OM **2009** *28* 2915



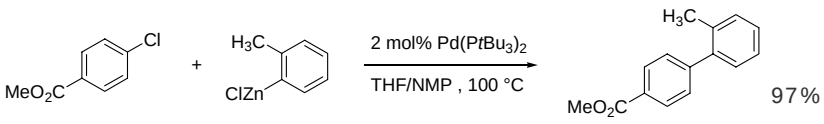
Buchwald *JACS* **2007** *129* 3844

Corriu *JCS Chem Comm* **1972** 144
Kumada *JACS* **1972** *94* 4374

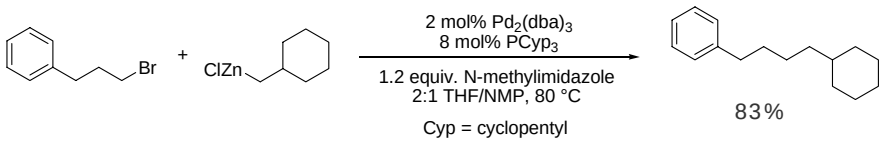
Negishi Coupling



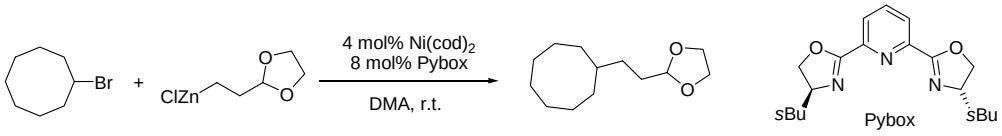
Kibayashi *JOC* **2002** *67* 5517



Fu *JACS* **2001** *123* 2719



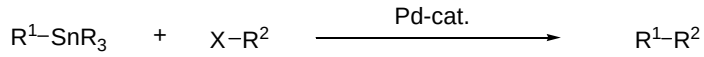
Fu *JACS* **2003** *125* 12527
Buchwald *JACS* **2009**
doi: 10.1021/ja902046m



Fu *JACS* **2003** *125* 14726

Negishi *JOC* **1977** *42* 1821
Acc Chem Res **1982** *15* 340

Stille Coupling



Typical conditions:

$Pd(Ph_3P)_4$, toluene, rfx
$PdCl_2(PhCN)_2$ or $PdCl_2(CH_3CN)_2$, DMF
$Pd_2(dba)_3$ or $Pd(OAc)_2$, phosphine

Additives: CuI, CsF

Ligands: tBu$_3$P, S-Phos, (furyl)$_3$P, AsPh$_3$, ...

- good functional group tolerance
- organostannanes stable
- organostannanes toxic

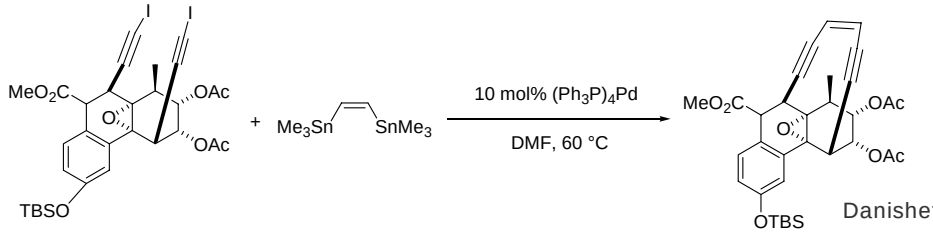
Initial Publications:

Migita *Chem Lett* **1977** 301, 1423
Stille *JACS* **1978** *100* 3636
JACS **1979** *101* 4992

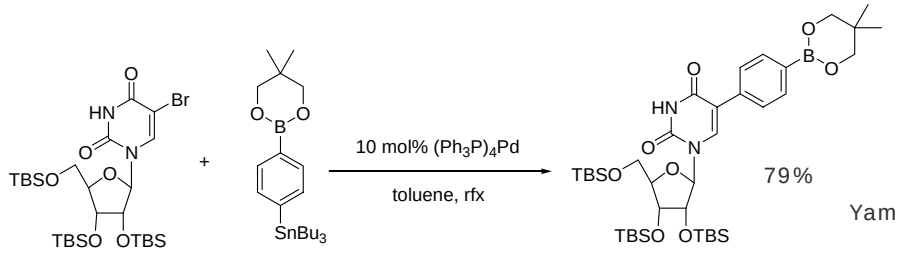
Reviews:

Stille *ACIEE* **1986** *25* 508
Mitchell *Synthesis* **1992** 803
Echavarren *ACIE* **2004** *43* 4704
ACIE **2005** *44* 3962

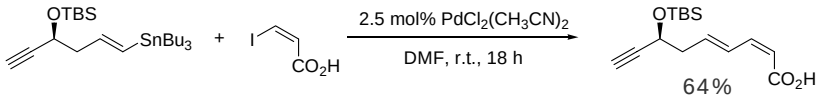
Stille Coupling



Danishefsky *JOC* **1994** *59* 3775

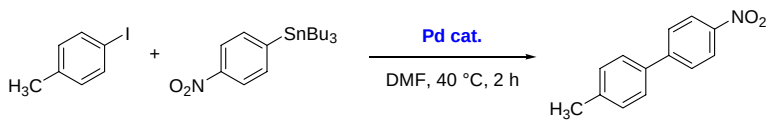


Yamamoto *JOC* **1989** *54* 4734



Smith *JACS* **1998** *120* 3935

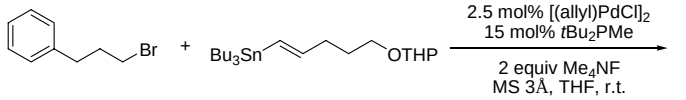
Stille Coupling



Catalyst

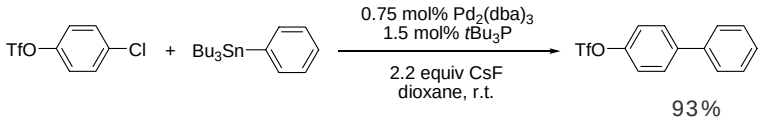
$(Ph_3P)_4Pd$	2%
$(Ph_3P)_4Pd$, CsF	8%
$(Ph_3P)_4Pd$, CuI	46%
$(Ph_3P)_4Pd$, CsF, CuI	**98%**

Baldwin *ACIE* **2004** *43* 1132



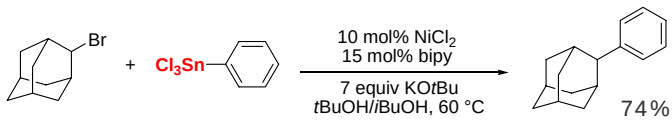
62%

Fu *JACS* **2003** *125* 3718



93%

Fu *JACS* **2002** *124* 6343



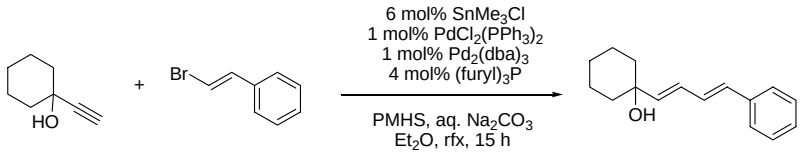
74%

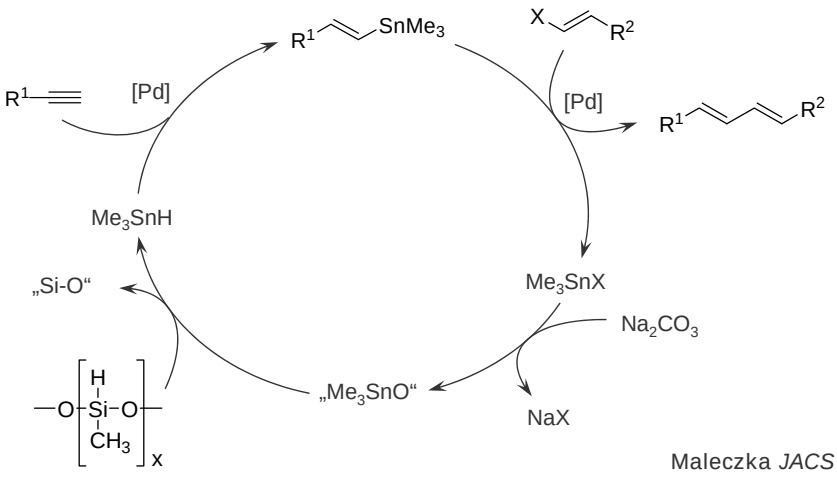
Fu *JACS* **2005** *127* 510

via radical mechanism

Stille Coupling

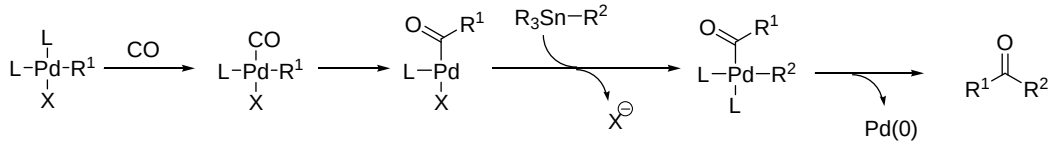
Catalytic in tin:

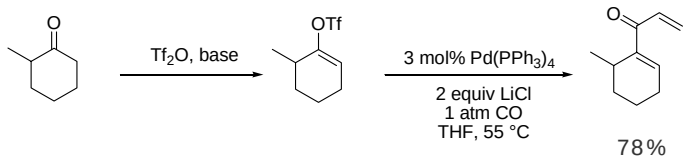




Maleczka *JACS* **2000** *122* 384

Carbonylative Stille Coupling

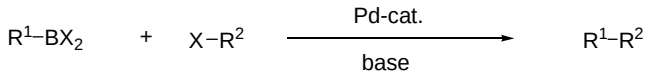




Stille *JACS* **1984** *106* 7500

Review: Beller *Angew Chem* **2009** *121* 4176

Suzuki Coupling



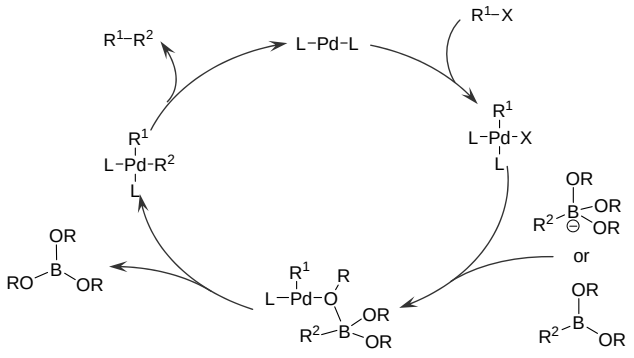
$R^1–BX_2$ = $R^1–B(OH)_2$ $R^1–B(OR)_2$ $R^1–BR_2$ $R^1–BF_3^{\ominus}$

- low toxicity
- boron compounds stable
- base required

Ligands: PPh_3, tBu$_3$P, S-Phos, NHC, …

Bases: aqueous: NaOH, KOH, Na_2CO_3, K_2CO_3,…
anhydrous: Cs_2CO_3, K_3PO_4, K_2CO_3, CsF

Solvents: THF, DME, dioxane, toluene, DMF



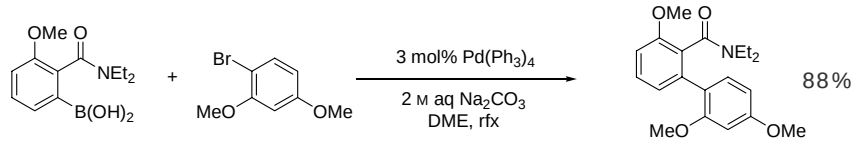
Initial Publications:

Suzuki *JCS Chem Commun* **1979** 866
THL **1979** 3437
Synth Commun **1981** *11* 513

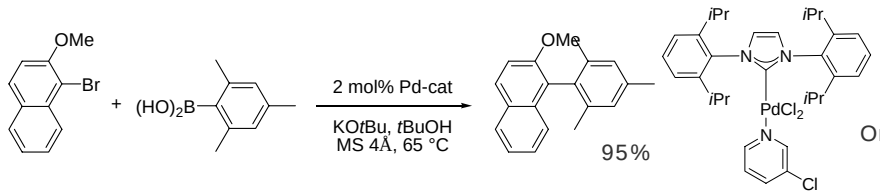
Reviews:

Suzuki *Chem Rev* **1995** *95* 2457
Danishefsky *ACIE* **2001** *40* 4544
Hassan *Chem Rev* **2002** *102 1359*
Miura *ACIE* **2004** *43* 2201
Beletskaya *TH* **2008** *64* 6047

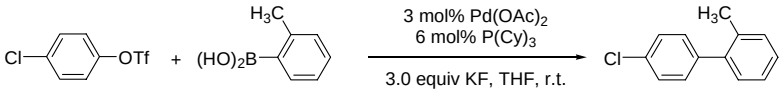
Suzuki Coupling

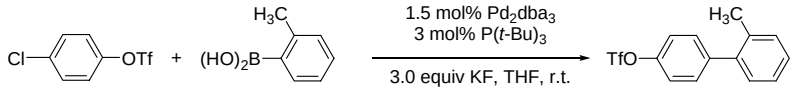


Sniekus *JOC* **1991** *56* 3763



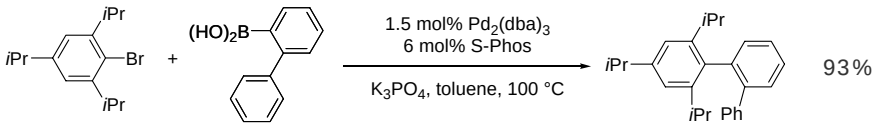
Organ *Angew Chem* **2009** *121* 2419

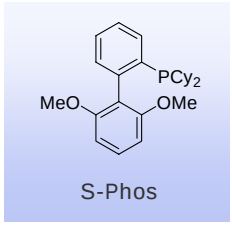


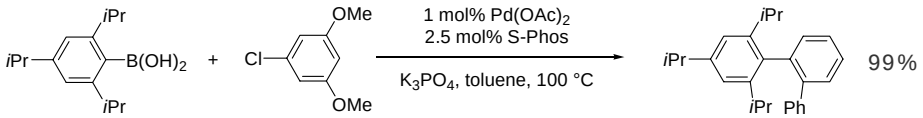


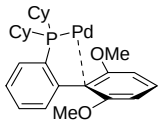
Fu *JACS* **2000** *122* 4020

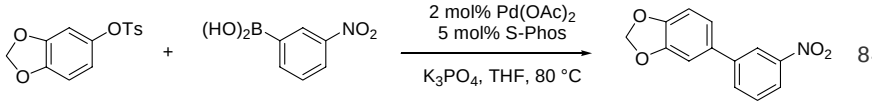
Suzuki Coupling







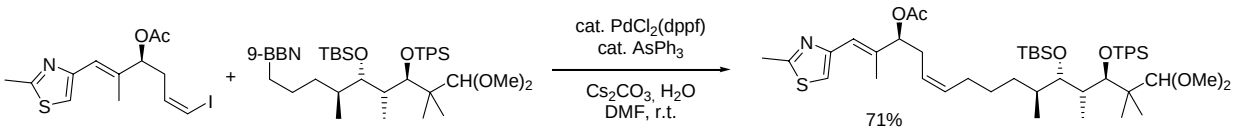




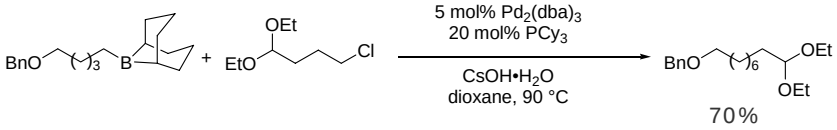
Buchwald *JACS* **1999** *121* 9550
JACS **2003** *125* 11818
ACIE **2004** *43* 1871
JACS **2005** *127* 4685

cf. Glorius *ACIE* **2003** *42* 3690

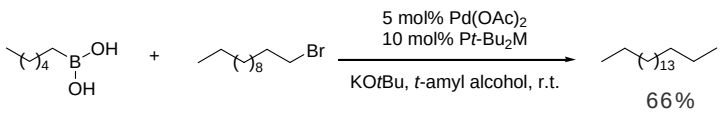
Suzuki Coupling



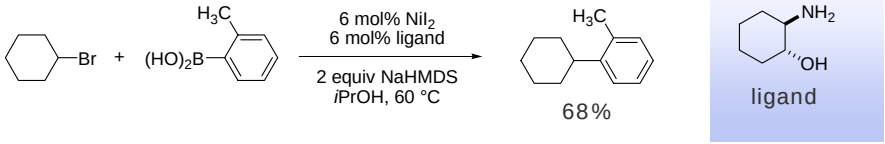
Danishefsky *ACIEE* **1996** *35* 2801
cf. Fürstner *Synlett* **2001** 290



Fu *JACS* **2001** *123* 10099
ACIE **2002** *41* 1945

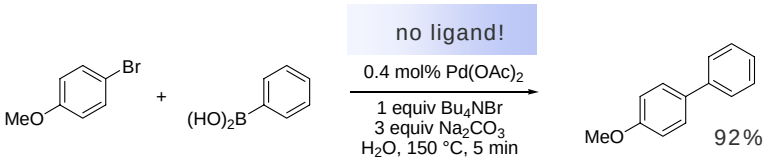


Fu *ACIE* **2002** *41* 3910
JACS **2002** *124* 13662

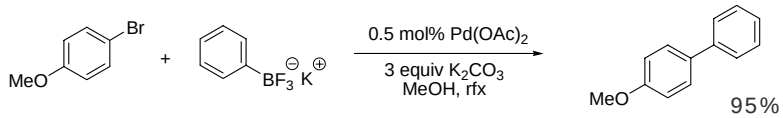


Fu *JACS* **2004** *126* 1340
JACS **2006** *128* 5360

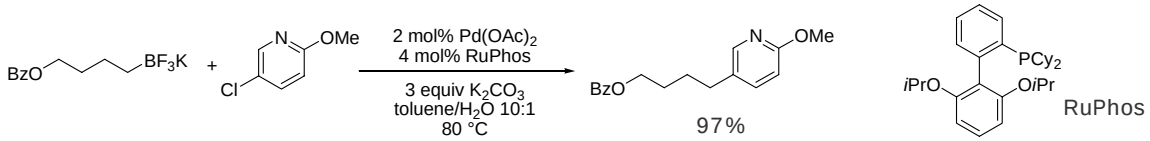
Suzuki Coupling



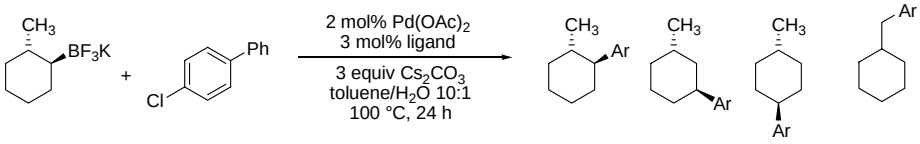
Leadbeater *JOC* **2003** *68* 888
JOC **2005** *70 161*



Molander *JOC* **2003** *68* 4302
Buchwald *OL* **2004** *6* 2649



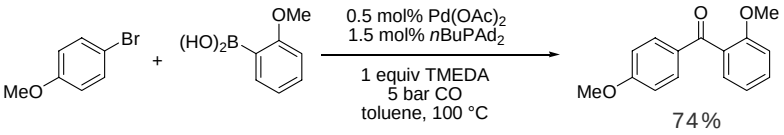
Molander *JOC* **2009** *74* 3626



*n*BuPAd$_2$	50	11	23	16
*t*Bu$_3$P	67	4	4	25
*t*Bu$_2$PPh	72	4	3	21

Molander *JACS* **2008** *130* 9257
Acc Chem Res **2007** *40* 275

Suzuki Coupling



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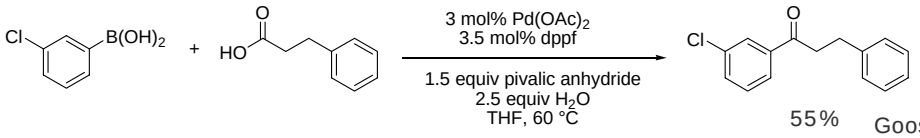
Beller *Chem Eur J* **2008** *14* 3645
cf. Suzuki *THL* **1993** *34* 7595



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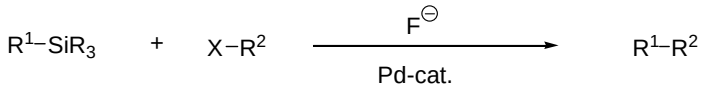
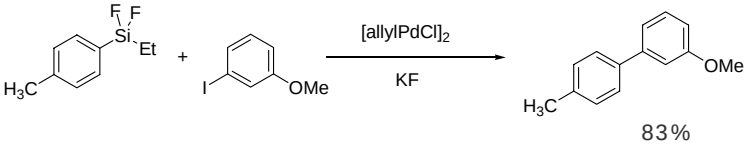
Goossen *ACIE* **2001** *40* 3458
Chem Comm **2001** 2084
Synlett **2002** 1237

Hiyama Coupling





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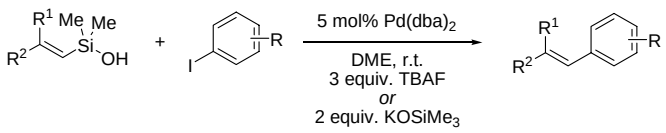
Hiyama *JACS* **1991** *113* 7075



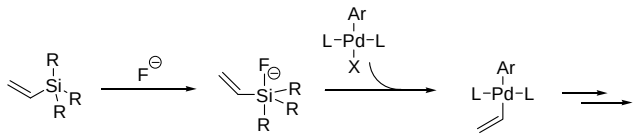
Denmark *JACS* **2001** *123* 6439

- low toxicity of Si reagents
- vinylsilanes react faster than arylsilanes
- vinylsilanes react stereospecifically

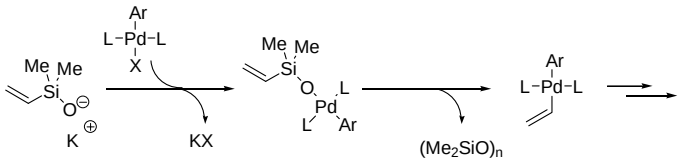
Hiyama *JOC* **1988** *53* 918
Denmark *Acc Chem Res* **2002** *35* 835
Denmark *Acc Chem Res* **2008** *41* 1486

Hiyama Coupling

Early mechanistic assumption:

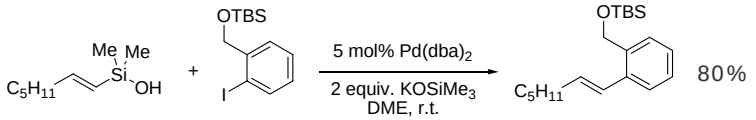


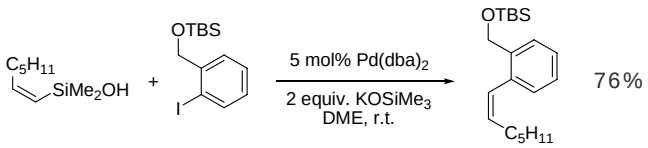
Revised mechanistic proposal:



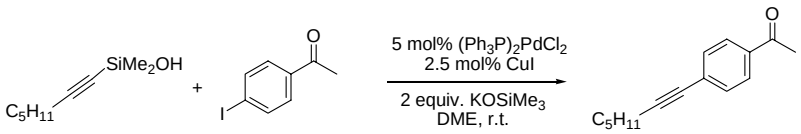
Denmark *JACS* **2004** *126* 4876

Hiyama Coupling

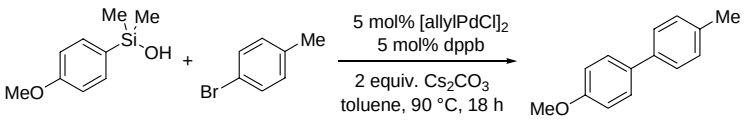




Denmark *JACS* **2001** *123* 6439

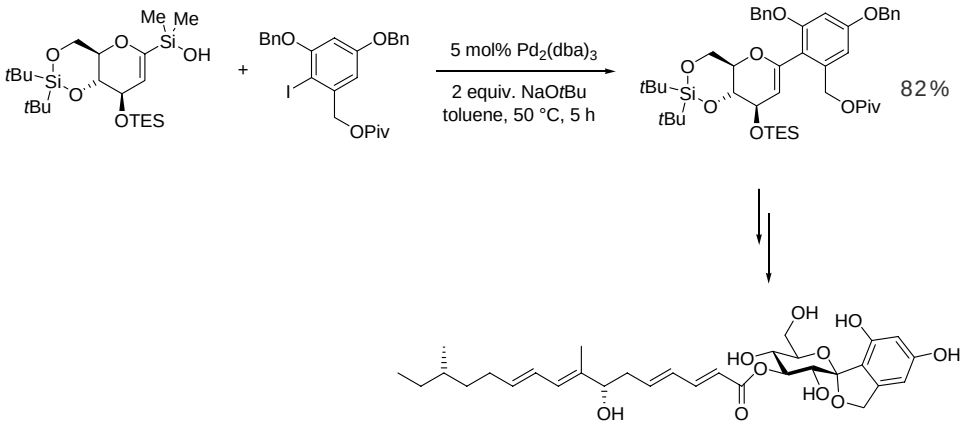


Denmark *JOC* **2003** *68* 9151



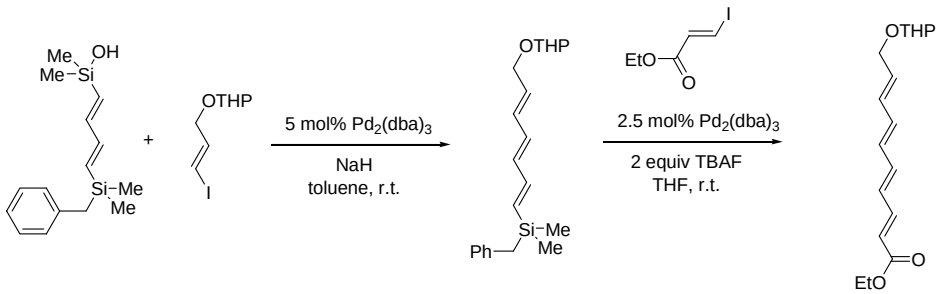
Denmark *OL* **2003** *5* 1357

Hiyama Coupling



papulacandin D

Hiyama Coupling



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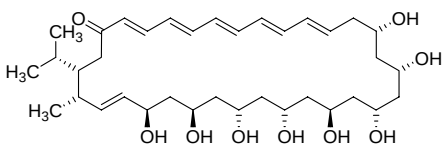

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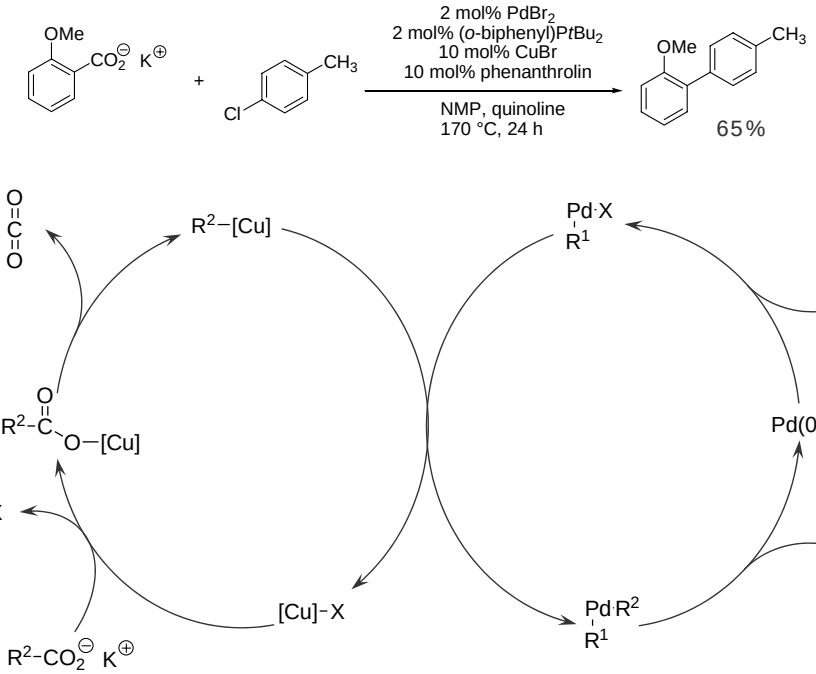
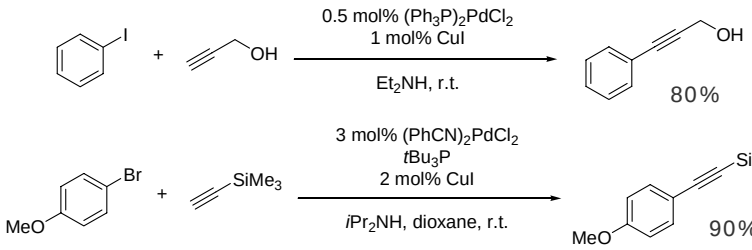
Denmark *JACS* **2005** *127* 8971

Decarboxylative Coupling



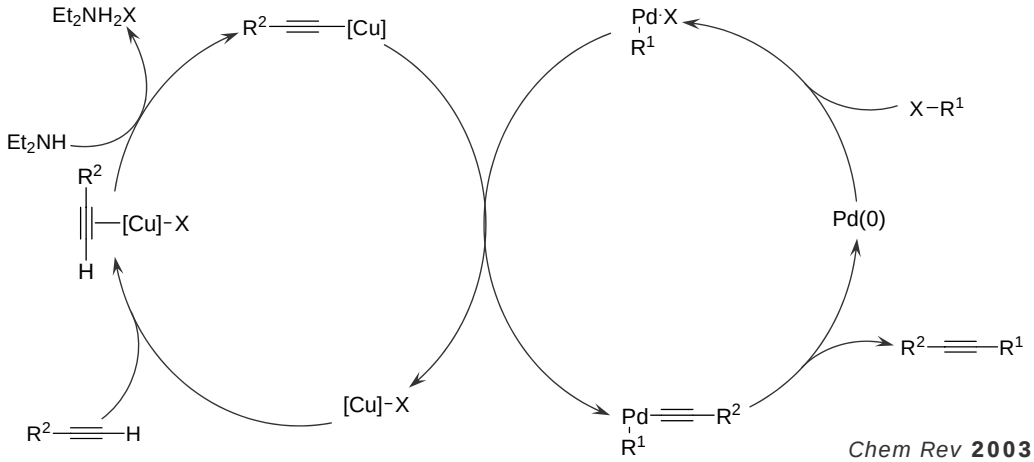
Goossen *Angew Chem* **2008** *120* 7211
Science **2006** *313* 662

Sonogashira Reaction



Sonogashira *THL* **1975** 4467

Fu *OL* **2000** *2* 1729
Buchwald *ACIE* **2003** *42* 5993



Chem Rev **2003** *103* 1979