За что хотели бы дать и за что дали Нобелевскую премию 2005 года

Рождественская лекция
на Химическом факультете
МГУ, 26 декабря 2005

Владимир Николаевич Ипатьев

1867-1952

А.Е.Чичибабин

Алексей Евгеньевич Чичибабин

1871-1945

William S. Knowles

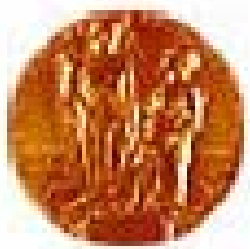
Ryoji Noyori

K. Barry Sharpless

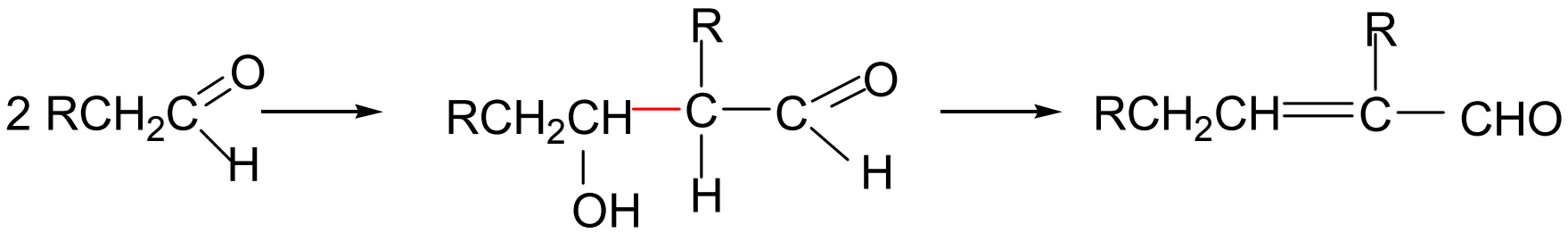
"For their work on chirally catalysed hydrogenation reactions"

"For his work on chirally catalysed oxidation reactions"

2001



Альдольная конденсация

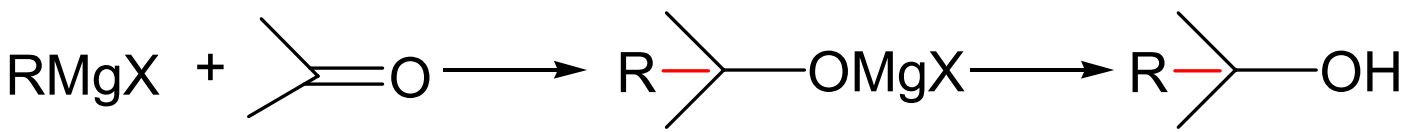


Реакции с участием реактива Гриньяра

Victor Grignard

Paul Sabatier

1912

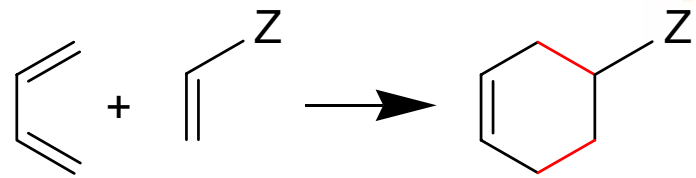


Реакция Дильса-Альдера

1950

Otto Paul Hermann Diels

Kurt Alder

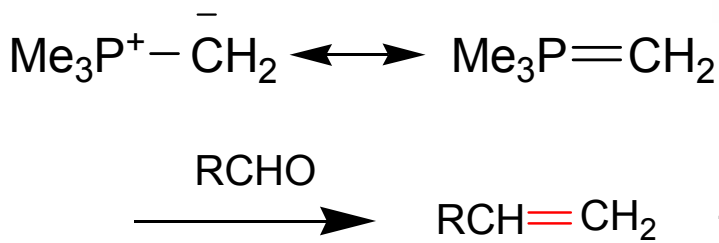


1979

Реакция Виттига

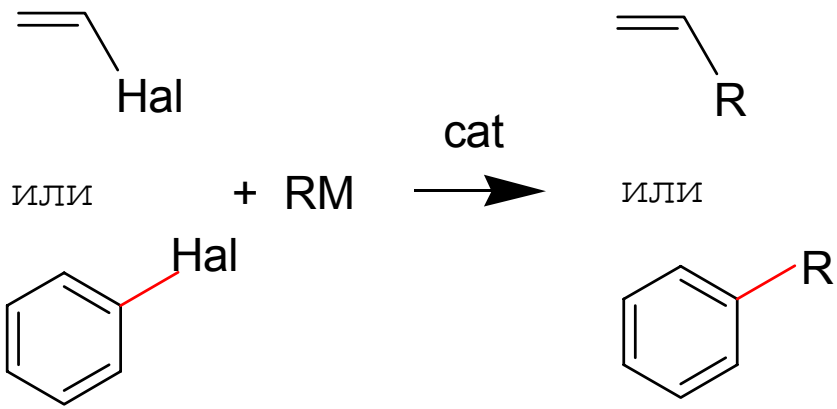
Herbert C. Brown

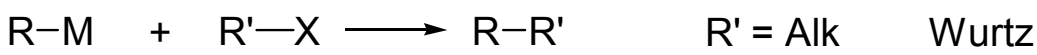
Georg Wittig

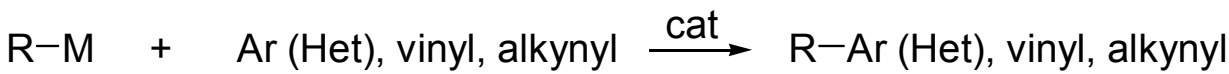


1972

Реакция кросс-сочетания



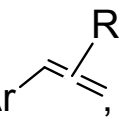
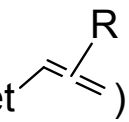




cat = Ni, Pd

Kumada, Corriu (1972)

aryl—aryl (Ar-Ar, Ar-Het, Het-Het)

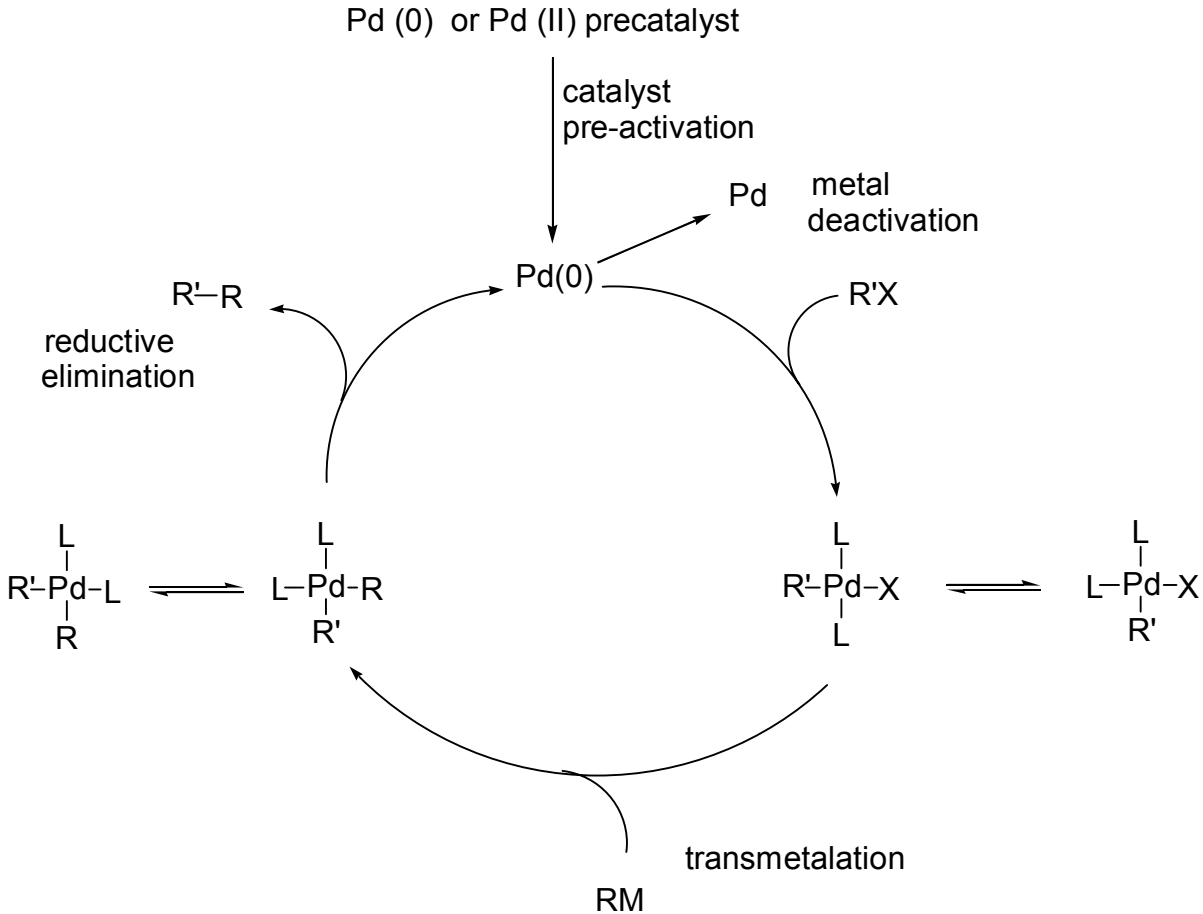
aryl—alkenyl (Ar  , Het )

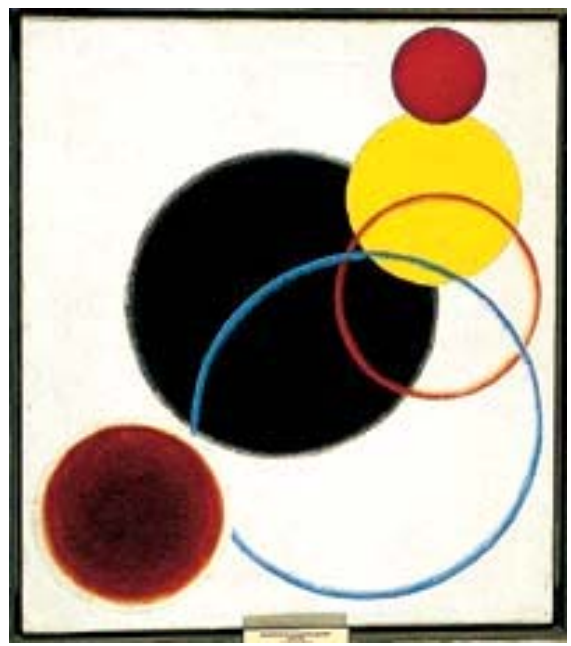
alkenyl—alkenyl

aryl—alkynyl (Ar —≡—R, Het —≡—R)

alkenyl—alkynyl

aryl—alkyl


Pd (0) or Pd (II) precatalyst
catalyst
pre-activation
Pd
metal
deactivation
Pd(0)
R'–R
reductive
elimination
R'X
L
R'–Pd–L
R
L
L–Pd–R
R'
L
R'–Pd–X
L
L
L–Pd–X
R'
transmetalation
RM



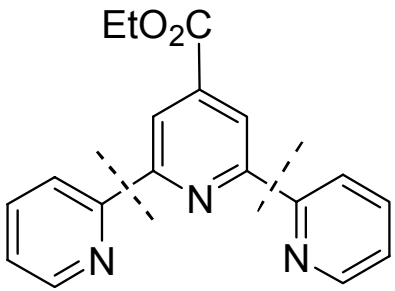
Kosugi-Migita-Stille reaction

$RSnBu_3$ + Ar(Het)X or alkenylX

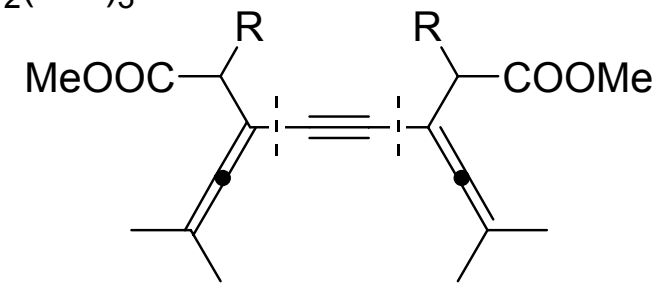
R = Ar, Het, alkenyl, alkynyl

$Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $Pd_2(dba)_3/AsPh_3$

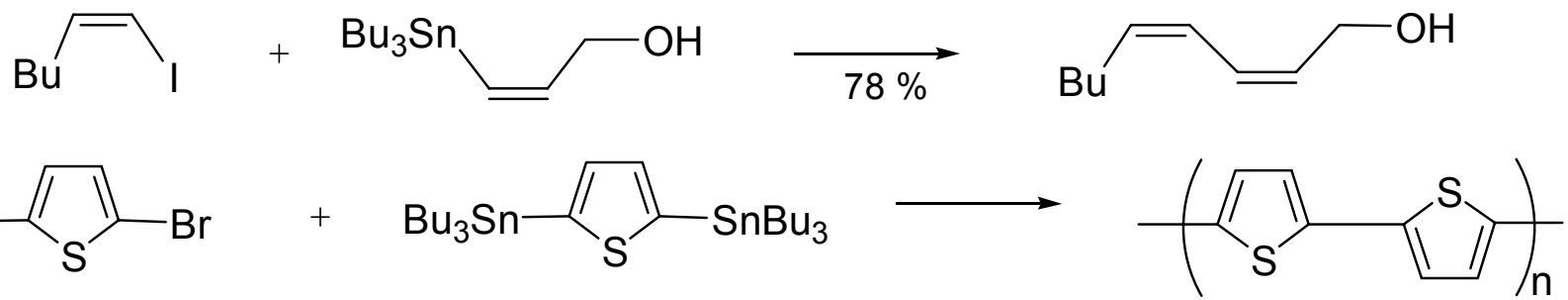
$PdCl_2(MeCN)_2$, $Pd(OAc)_2$, $Pd_2(dba)_3$



(toluene, reflux)

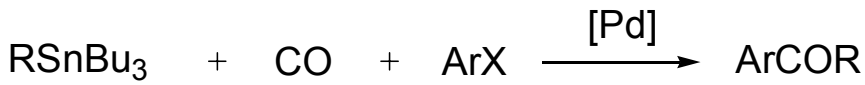


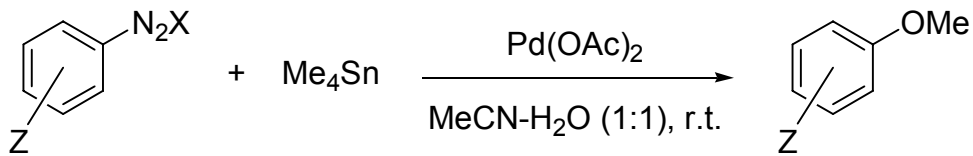
(NMP, r.t.)

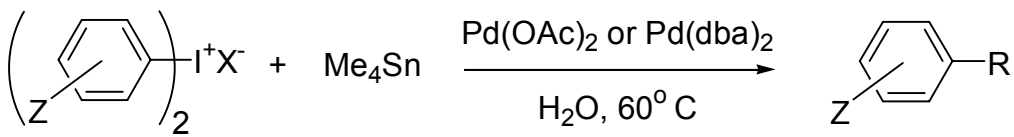


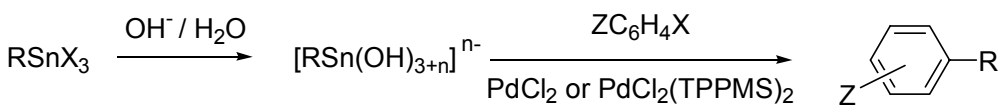

Bu3Sn−SnBu3 + RBr [Pd] RSnBu3

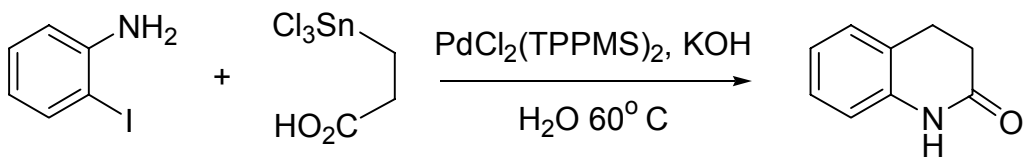

ArSnBu3 + RCOCl [Pd] ArCOR

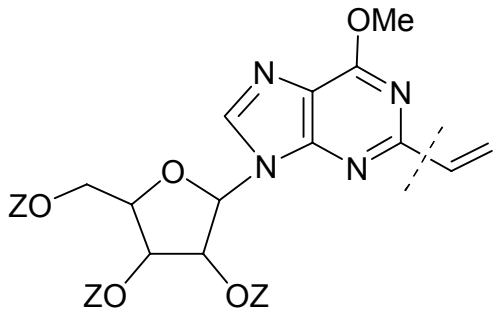

RSnBu3 + CO + ArX [Pd] ArCOR

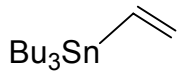

N2X
Z
+ Me4Sn
Pd(OAc)2
MeCN-H2O (1:1), r.t.
OMe
Z


I+X-
Z
2
+ Me4Sn
Pd(OAc)2 or Pd(dba)2
H2O, 60° C
Z
R

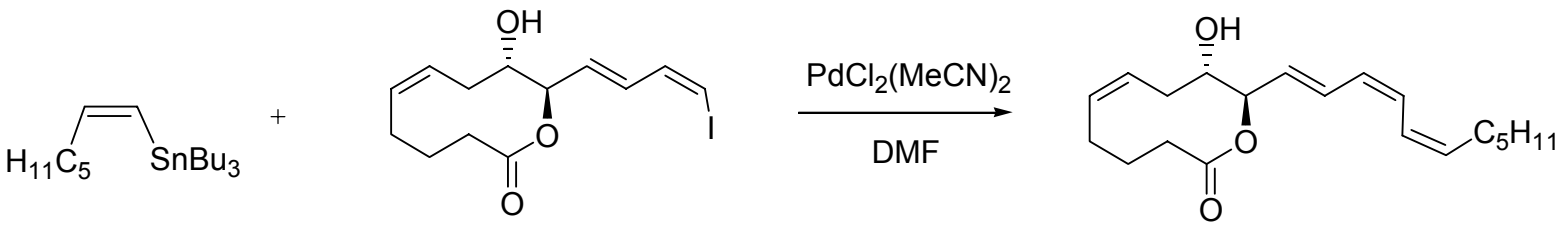

RSnX3
OH- / H2O
[RSn(OH)3+n] n-
ZC6H4X
PdCl2 or PdCl2(TPPMS)2
Z
R


NH2
I
+
Cl3Sn
HO2C
PdCl2(TPPMS)2, KOH
H2O 60° C
N
H
O

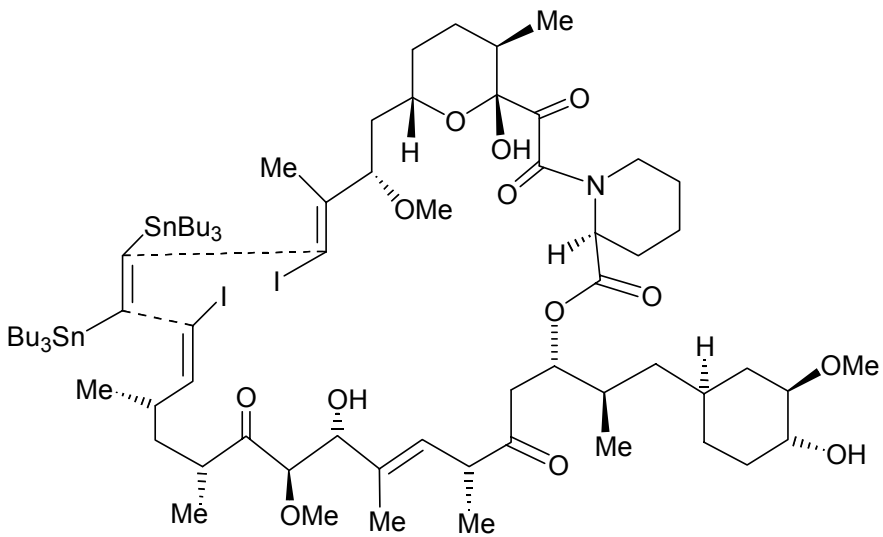




$PdCl_2(MeCN)_2$, toluene



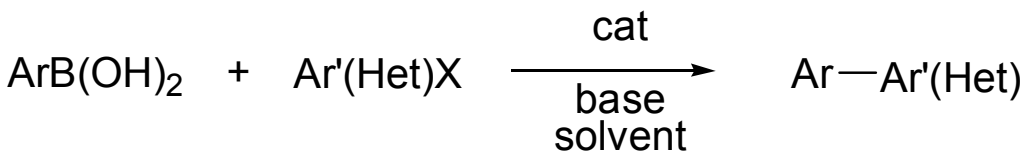
ascidiatrienolide



28%

$PdCl_2(MeCN)_2$, DMF-THF,
i-Pr_2NH

Suzuki-Miyaura reaction

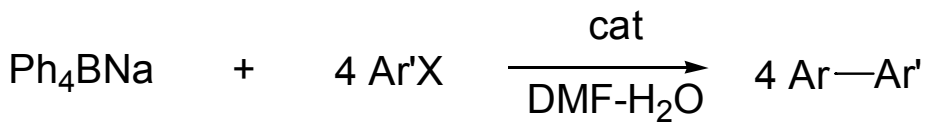


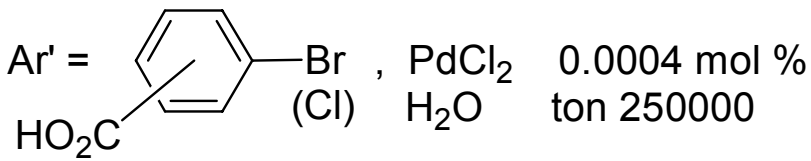
cat = $Pd(PPh_3)_4$, $Pd(OAc)_2$/L, $Pd(OAc)_2$, Pd-cluster

base = Na_2CO_3, K_2CO_3, Cs_2CO_3, KF, K_3PO_4, PhONa, $Ba(OH)_2$, TlOH

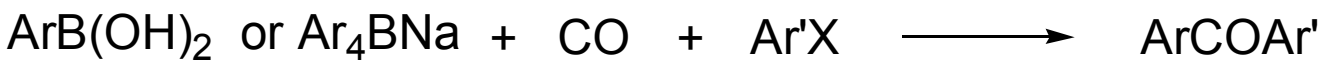
solvent = DMF, toluene, benzene, THF, dioxane, DMF-H_2O, PhMe-H_2O, H_2O

X = I, Br, Cl, OTf

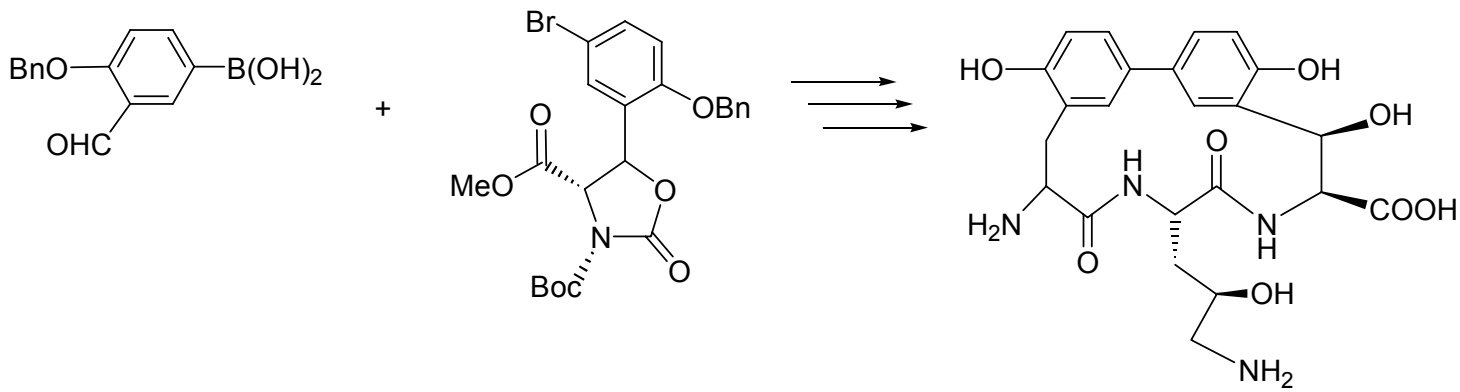

Ph4BNa + 4 Ar'X
cat
DMF-H2O
4 Ar—Ar'


Ar' =
Br
(Cl)
HO2C
, PdCl2
H2O
0.0004 mol %
ton 250000

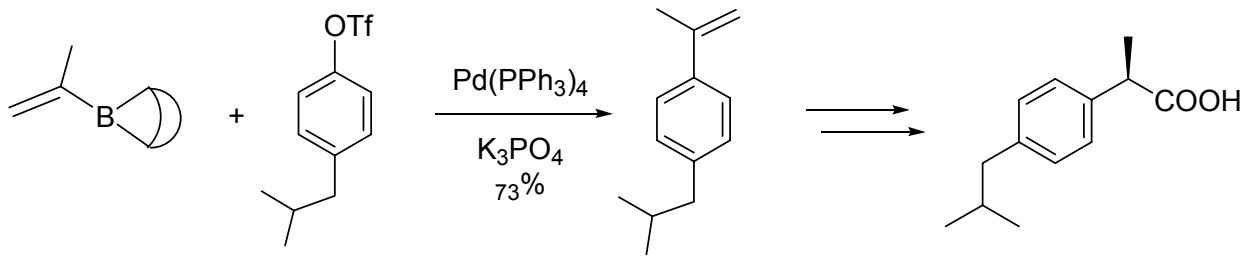

ArB(OH)2 + RCOCl
ArCOR


ArB(OH)2 or Ar4BNa + CO + Ar'X
ArCOAr'

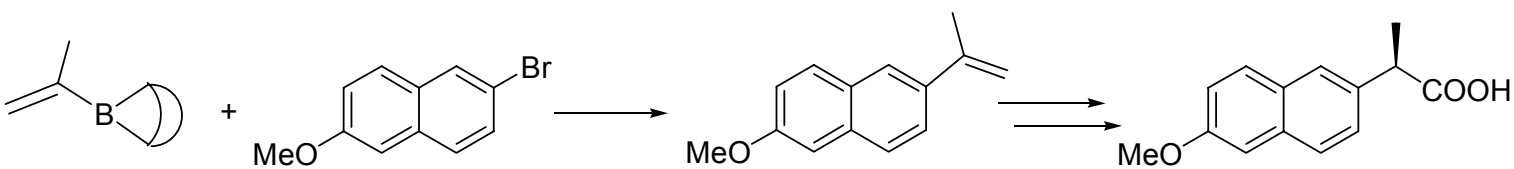
Natural products



biphenomycin A

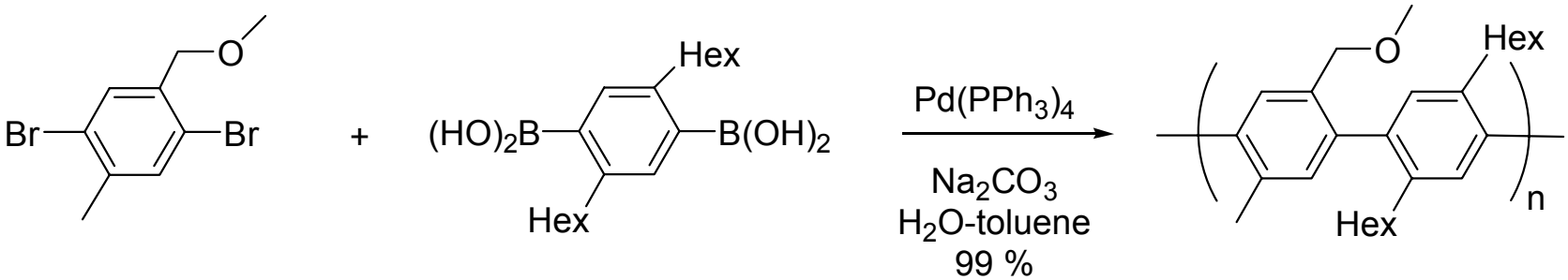


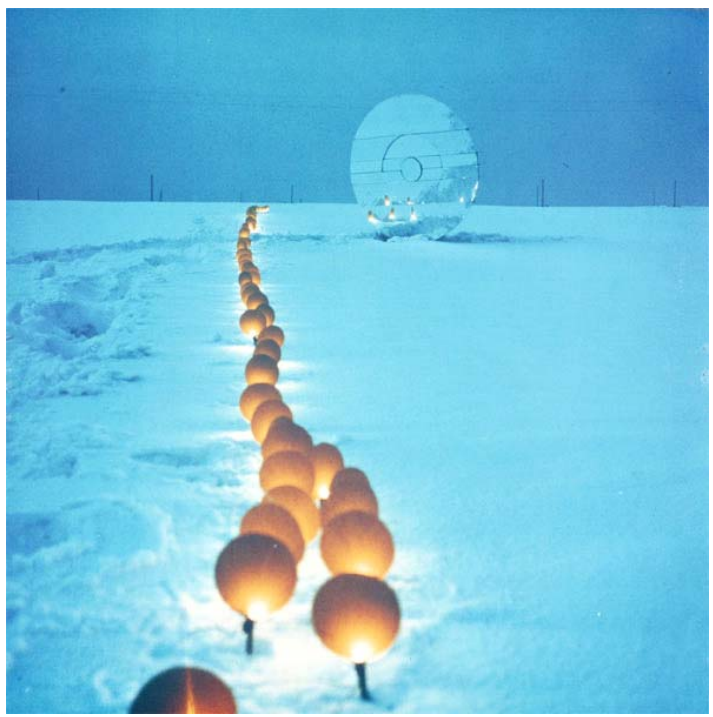
ibuprofen



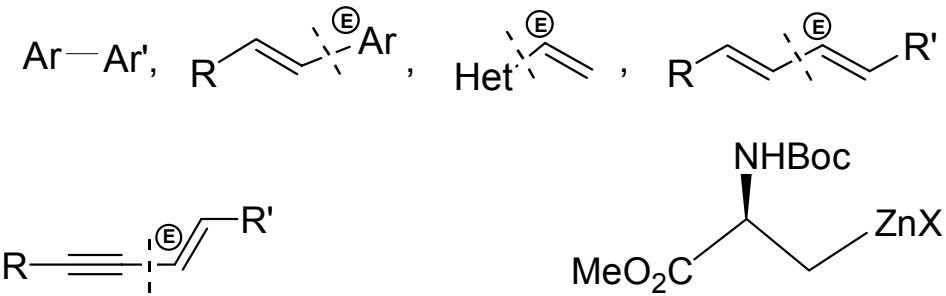
S-naproxen

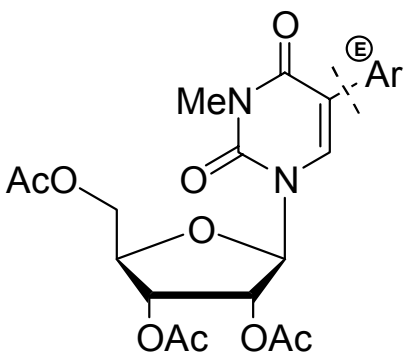
Polymers


O
Br
Br
+
Hex
(HO)2B
B(OH)2
Hex
Pd(PPh3)4
Na2CO3
H2O-toluene
99 %
O
Hex
n
Hex

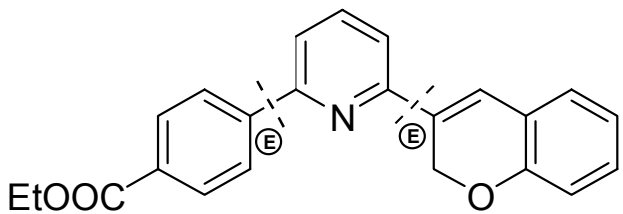


Negishi reaction

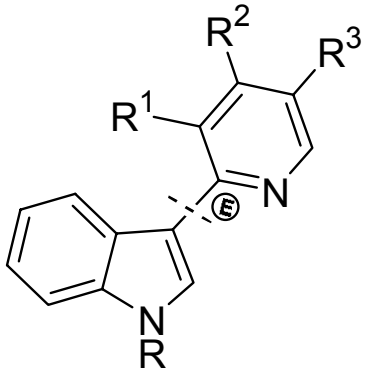




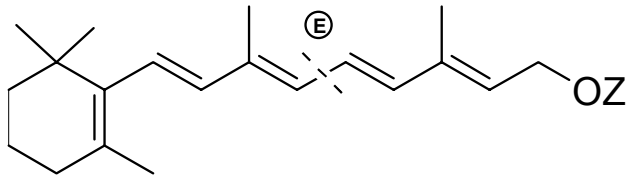
M = ZnI, X = I
$Pd_2(dba)_3$, $P(fur)_3$
THF, r.t., 58%



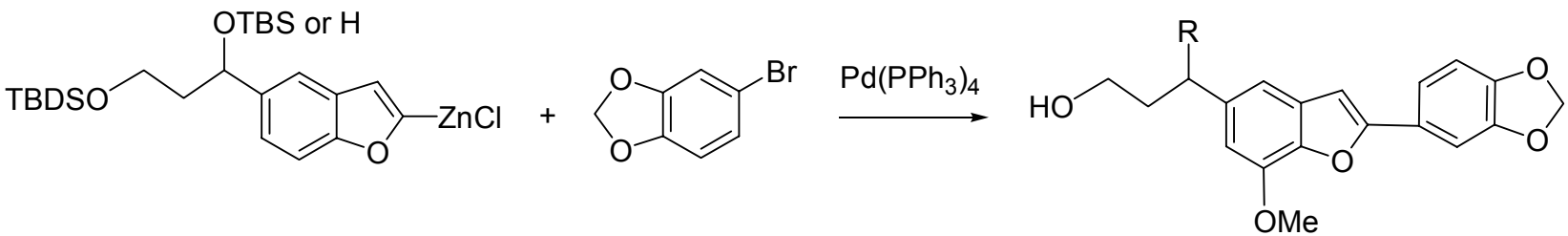
a. M = ZnBr, X = OTf;
b. M = ZnBr, X = I
$Pd(PPh_3)_2Cl_2$, THF-DME, 60°C



M = ZnCl, X = Cl or Br
$Pd(PPh_3)_2Cl_2$, DIBAL-H
THF, reflux



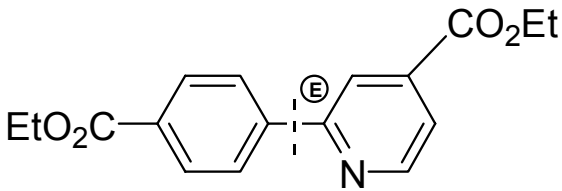
Z = $SiMe_2Bu^t$
M = $SiMe_3$ trace
$AlMe_2$ 41%
$AlMe_2$ + $ZnCl_2$ 60%



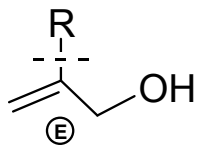
R = H egonol
R = OH (±) machicendiol

Tamao-Kumada reaction

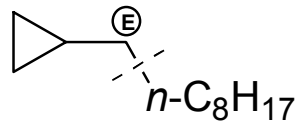
cat = Ni or Pd



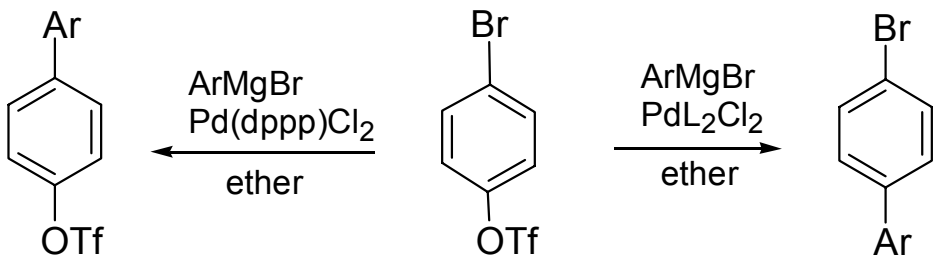
M = MgCl, X = Br
$Pd_2(dba)_3$, dppf
THF, - 20 °C

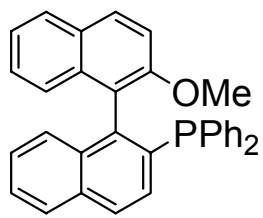


M = MgBr, X = Cl
$Ni(dppp)_2$, THF, reflux
R= Ph, Et, CH_2SiMe_3

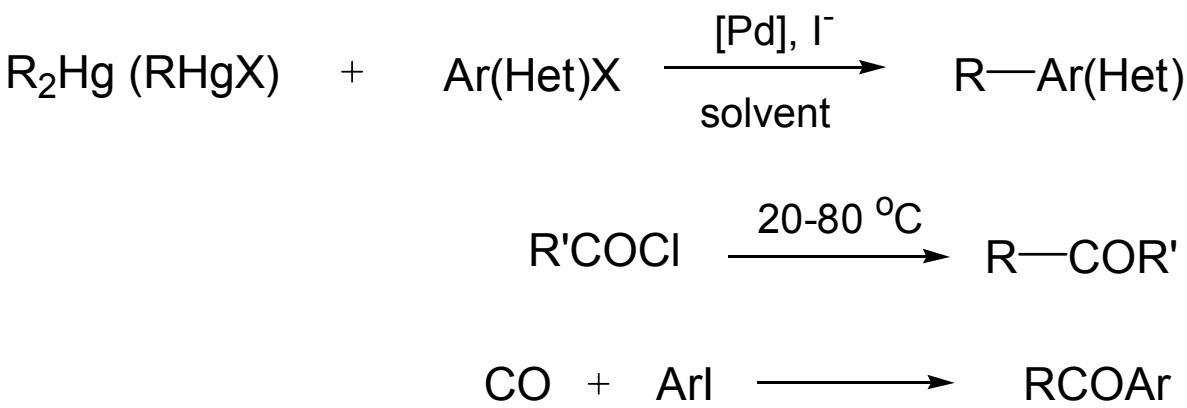


M = MgCl, X = Br
$NiCl_2$, C_4H_6, 0°C

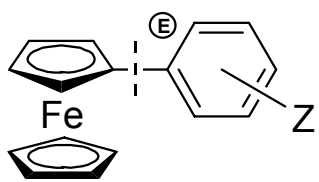


L = 

Other nucleophilic reagents (M= Hg, Cu, Al, Ga, Ti, Zr, Bi, Mn)

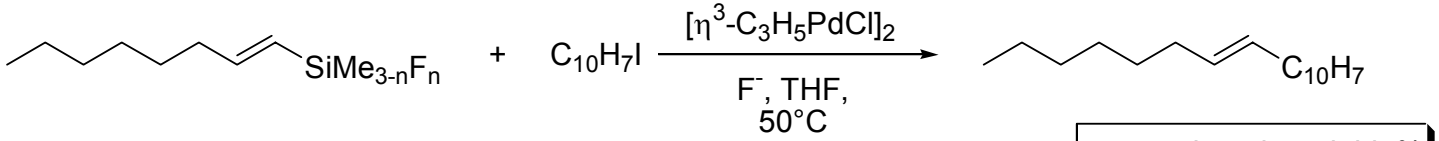


R = Ar, Het, Alk
solvent = HMPA, DMF, THF, Me_2CO, MeCN, Ph

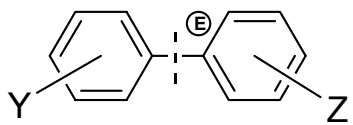


M = Hg, X = I
$PdCl_2(PPh_3)_2$, NaI
Me_2CO-THF, reflux

Hiyama-Hatanaka reaction

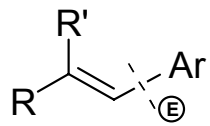


n	time, h	yield, %
0	24	0
1	10	81
2	48	74
3	24	0

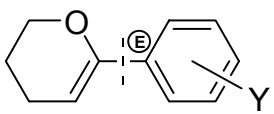


M = $SiMe_n(OH)_{3-n}$ (n=0,1,2), X = I
$Pd(PPh_3)_4$, Ag_2O, THF, reflux

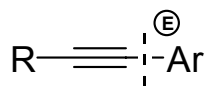
or M = $Si(OMe)_3$, X=Br, I
$Pd(OAc)_2$, PPh_3, TBAF
72-92%



M = $Si(OH)Me_2$, X=I
$Pd_2(dba)_3$, $KOSiMe_3$ or NaH
DME, r.t.
97-99%



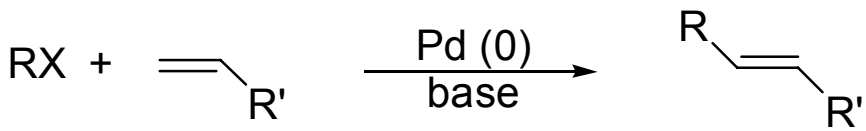
M = $SiMe_2OH$, X=I
$(\eta^3\text{-}C_3H_5PdCl)_2$, TBAF
THF, r.t.
74-92%



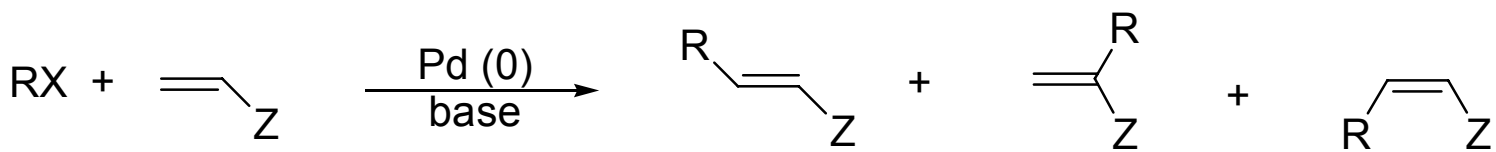
M = $Si(OH)Me_2$, X=I
$Pd(PPh_3)_4$, TBAF or Ag_2O
THF, 60°C
52-99%

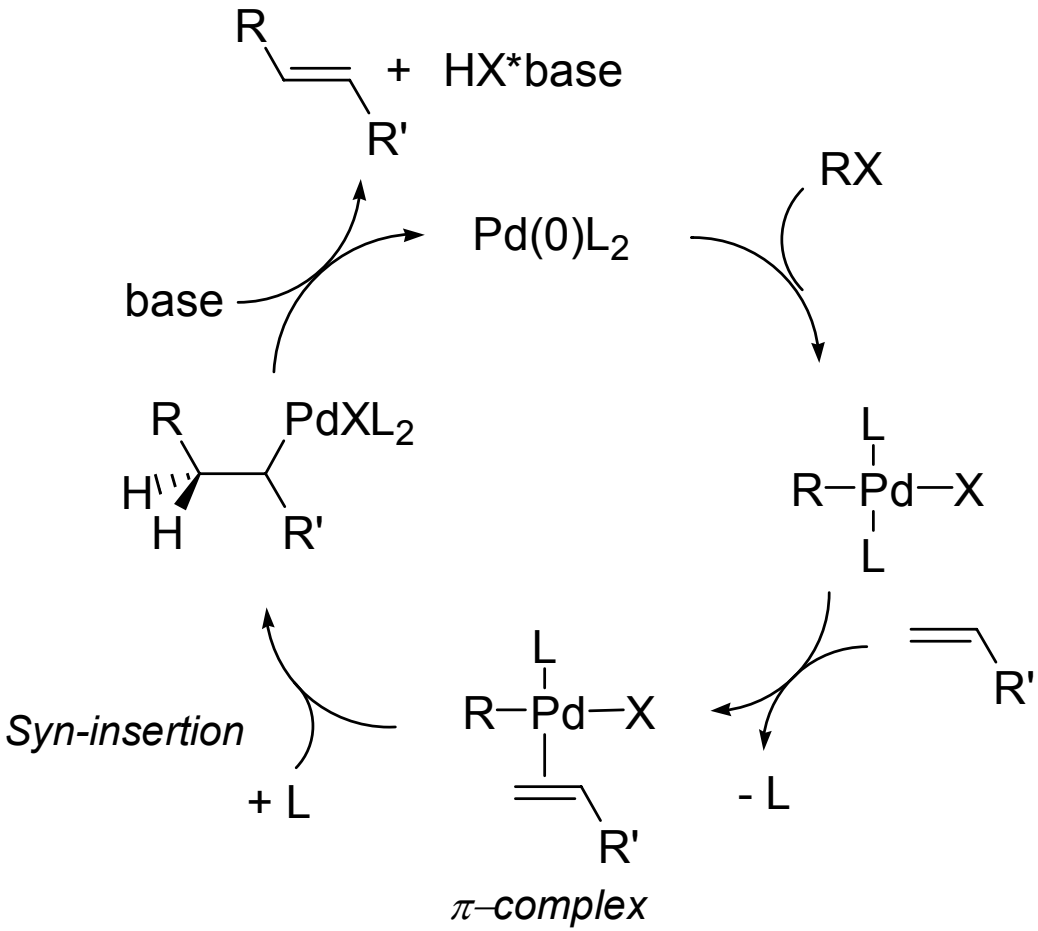
СООБЩЕСТВО

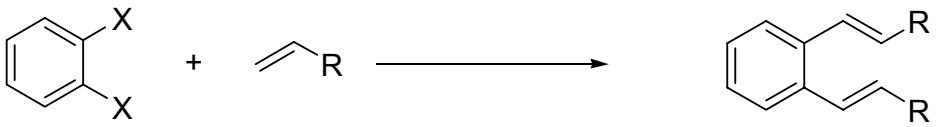
The Mizoroki – Heck Reaction

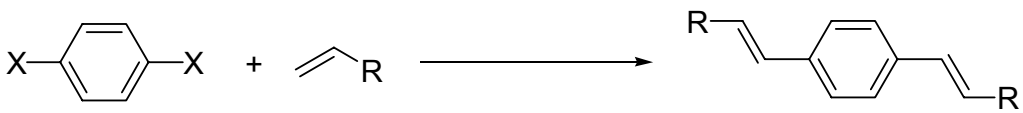


R = Ar, vinyl, Bn
X = I, Br, OTf, etc.
R' = CHO, CN, CO_2Me, SO_2NH_2, $P(O)(OEt)_2$




R
+ HX*base
R'
RX
Pd(0)L2
base
R
PdXL2
H
H
R'
L
R–Pd–X
L
R'
- L
L
R–Pd–X
R'
π–complex
Syn-insertion
+ L

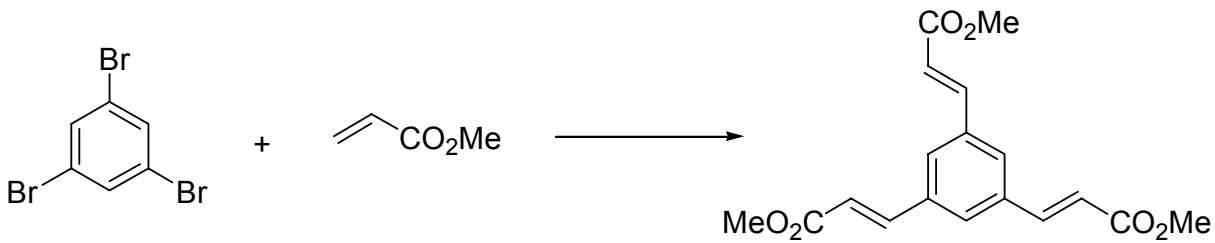




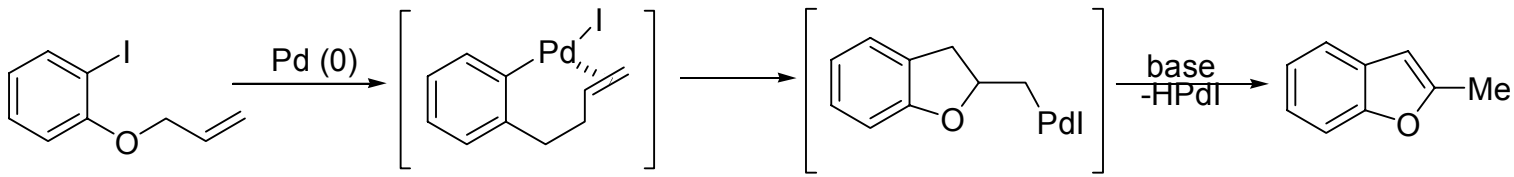
R = Ph, X = I 67%
$Pd(OAc)_2$, Bu_3N, 100 ^oC, 72 h

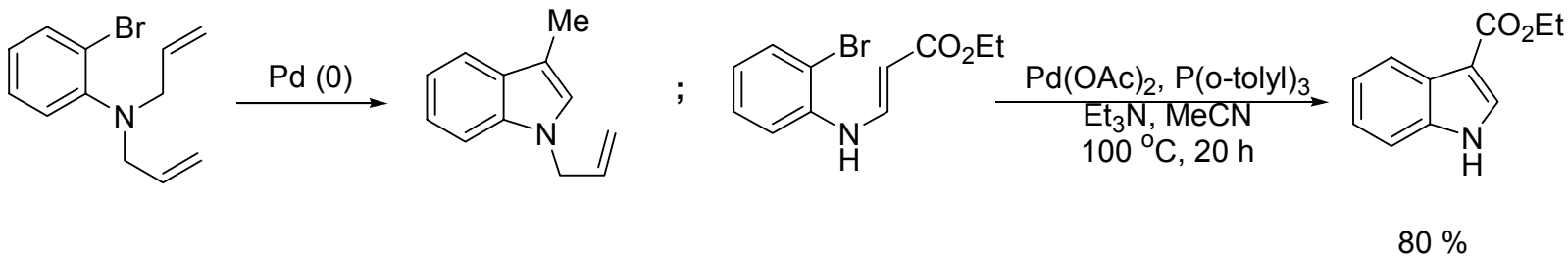
R = Ph, X = I 70%
$PdCl_2(PPh_3)_2$, Bu_3N, K_2CO_3, H_2O 100 ^oC, 5 h

R = Ph, X = Br 85%
$PdCl_2(P(o\text{-}tolyl)_3)_2$, Bu_3N, K_2CO_3, H_2O 100 ^oC, 6 h

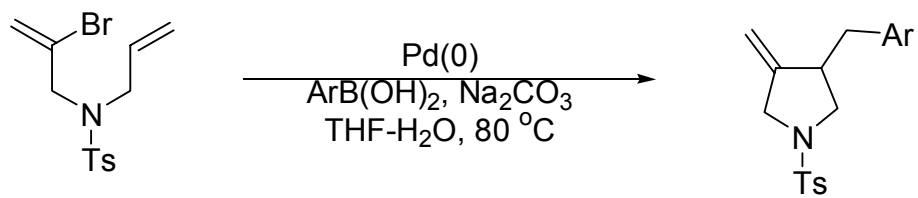


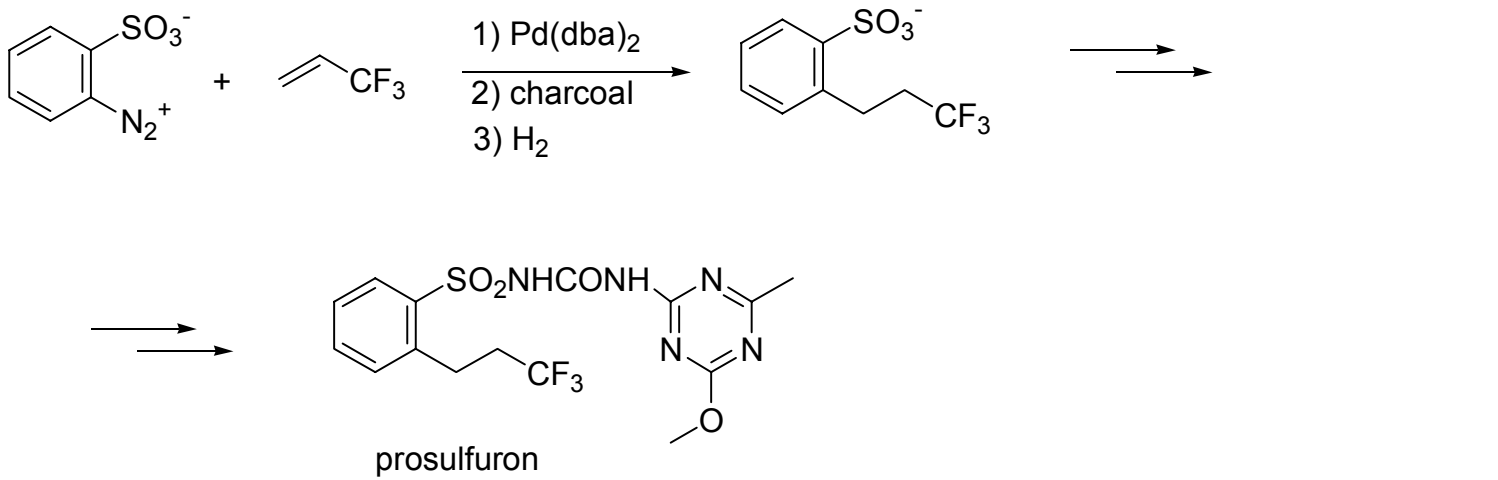
$Pd(OAc)_2$, $P(o\text{-}tolyl)_3$, Et_3N, MeCN, 80 ^oC, 5 h 63 %


I
Pd (0)
Pd
I
O
PdI
base
-HPdI
Me
O

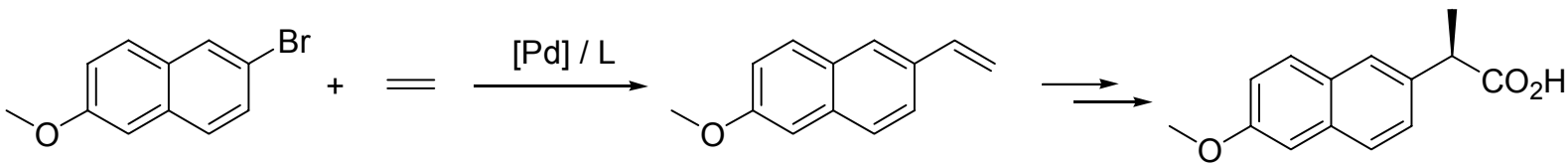

Br
N
Pd (0)
Me
N
;
Br
CO2Et
N
H
Pd(OAc)2, P(o-tolyl)3
Et3N, MeCN
100 °C, 20 h
CO2Et
N
H

80 %


Br
N
Ts
Pd(0)
ArB(OH)2, Na2CO3
THF-H2O, 80 °C
Ar
N
Ts



prosulfuron



The Nobel Prize in Chemistry 2005

"for the development of the metathesis method in organic synthesis"

Yves Chauvin

1/3 of the prize

France

Institut Français du Pétrole
Rueil-Malmaison, France

b. 1930

Robert H. Grubbs

1/3 of the prize

USA

California Institute of Technology (Caltech)
Pasadena, CA, USA

b. 1942

Richard R. Schrock

1/3 of the prize

USA

Massachusetts Institute of Technology (MIT)
Cambridge, MA, USA

b. 1945

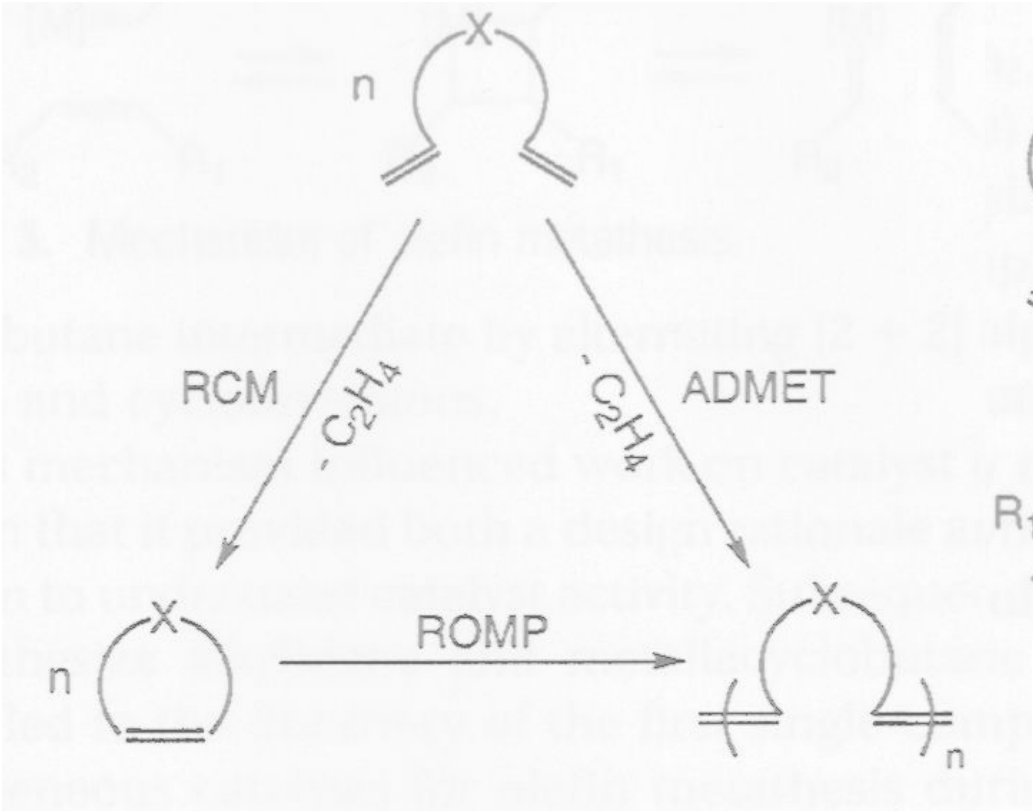
The alkene-metathesis reaction has developed into one of the most powerful carbon-carbon bond forming reactions currently available to the synthetic chemists.

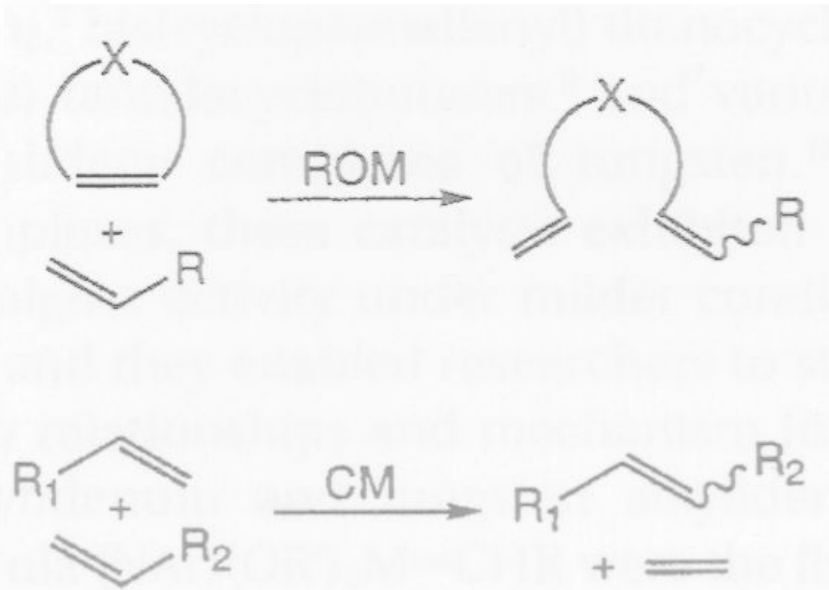
K.C.Nicolaou

Ring opening metathesis polymerisation reactions are widely used in the industrial production of polymers of great commercial value.

(Angew. Chem. Int. Ed. 36 (1997) 2036)

"Olefin metathesis" (Calderon, 1967)





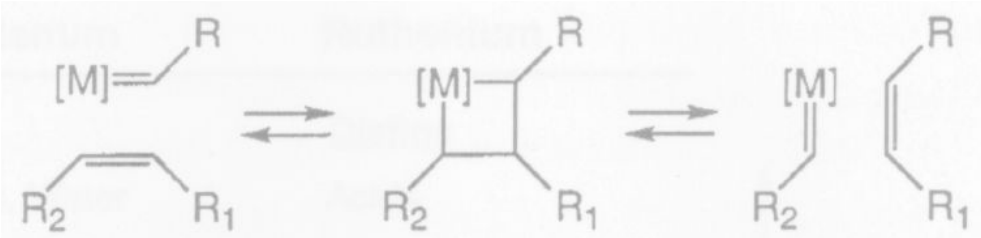
RCM – ring-closing metathesis

ADMET – acyclic diene metathesis polymerization

ROM – ring-opening metathesis

ROMP – ring-opening polymerization

CM – cross-metathesis

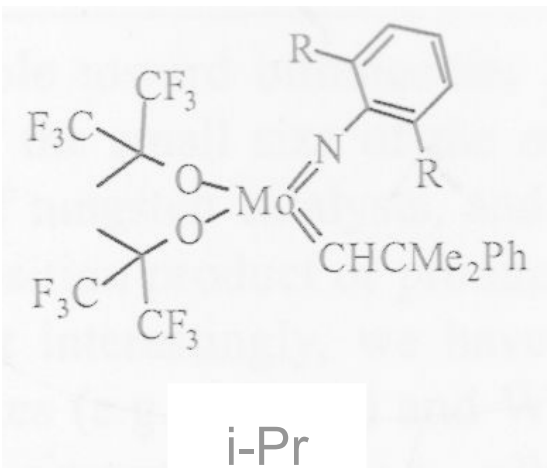


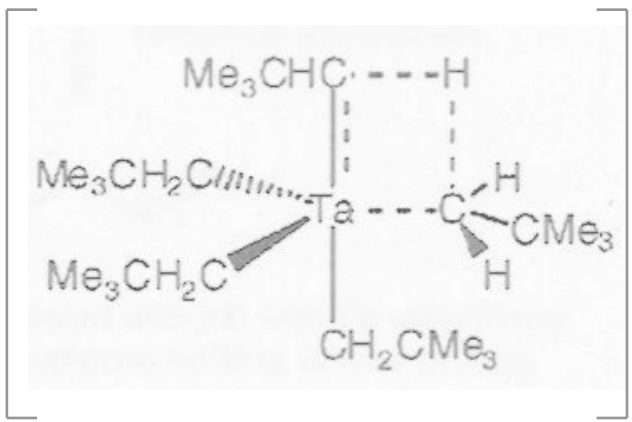
Ives Chauvin, 1970

$(CO)_5W{=}CPh_2$

$(NAr)(OR')_2M{=}CHR \quad \left(M{=}Mo,\ W\right)$

T.J.Katz ~1976 ; C.P.Casey ~ 1979

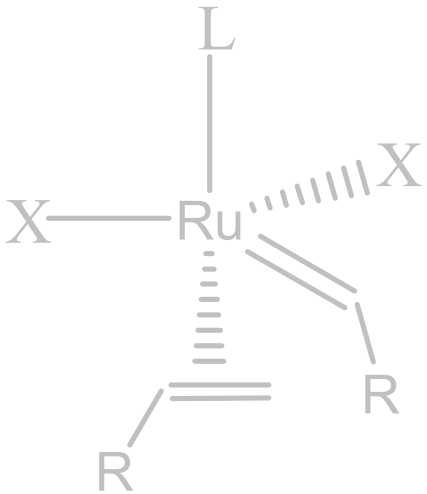


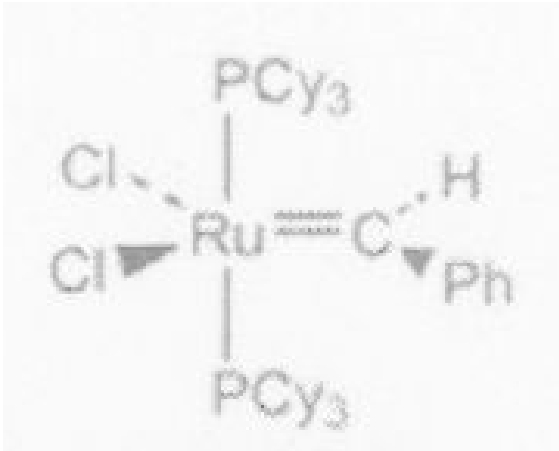


Richard R. Schrock, 1980-1990

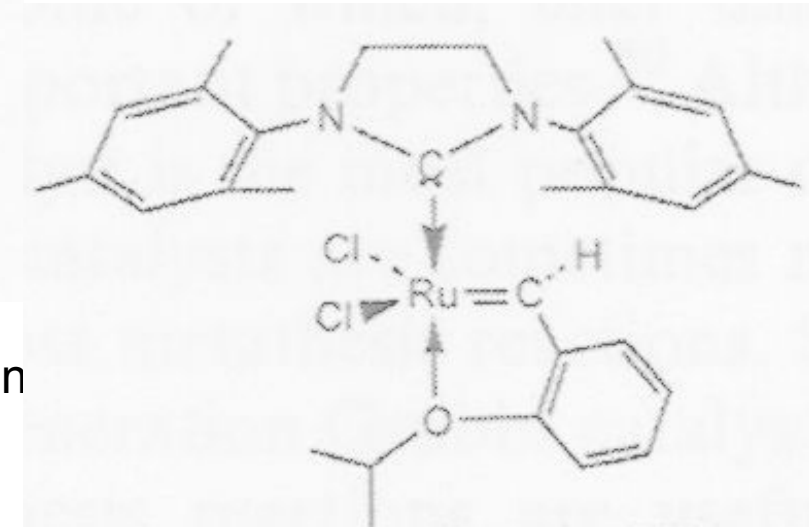
Design motif

Robert H. Grubbs, 1990 - 1995

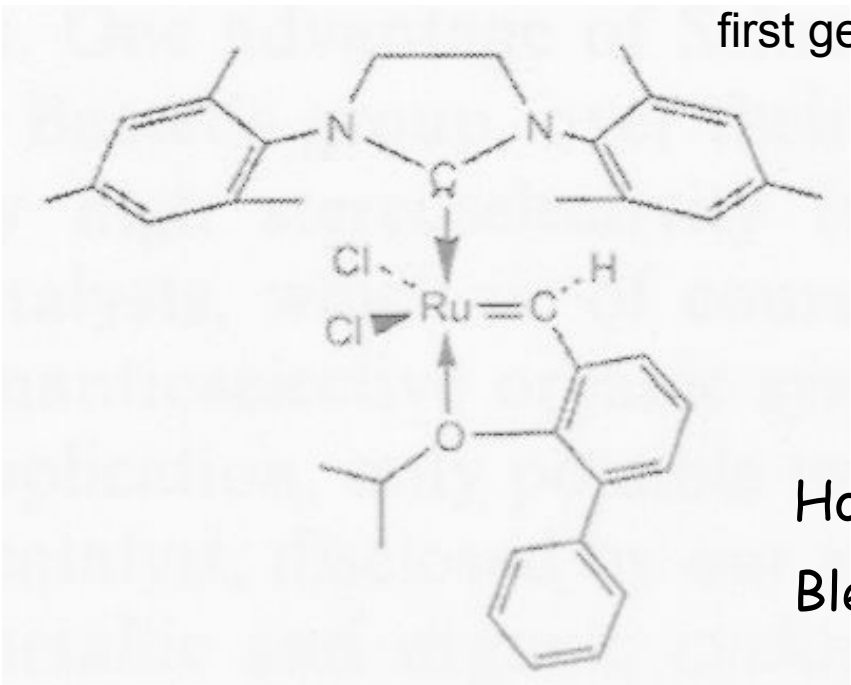




first generation



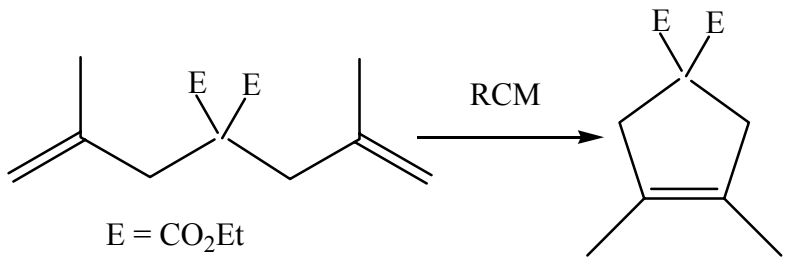
second generation

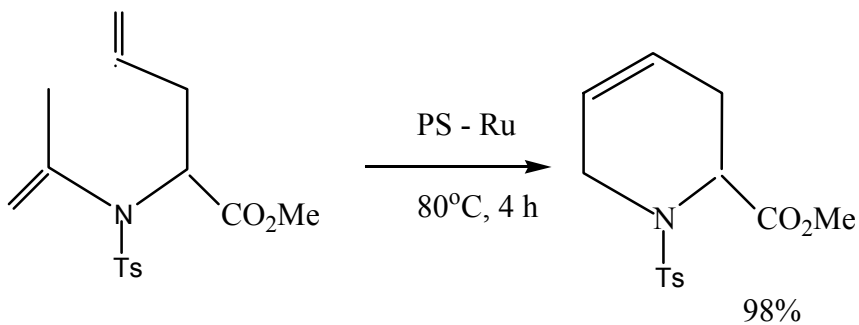


Hoveyda, 1999

Blechert, 2002

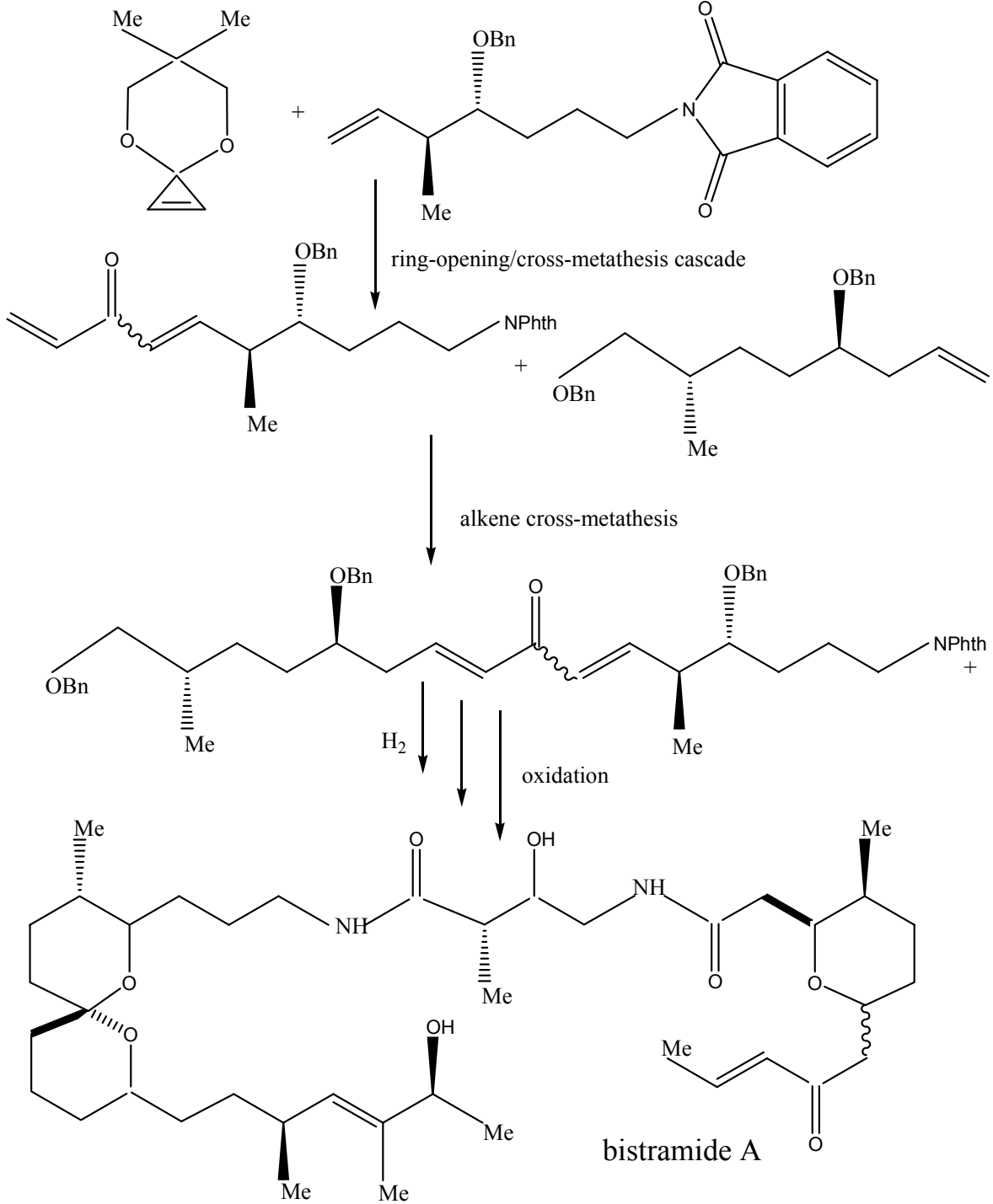
third generation (green catalyst)

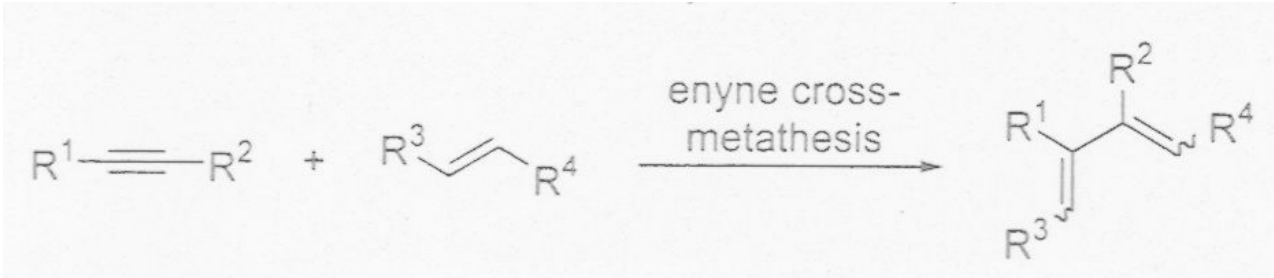

E
E
RCM
E
E
E = CO2Et

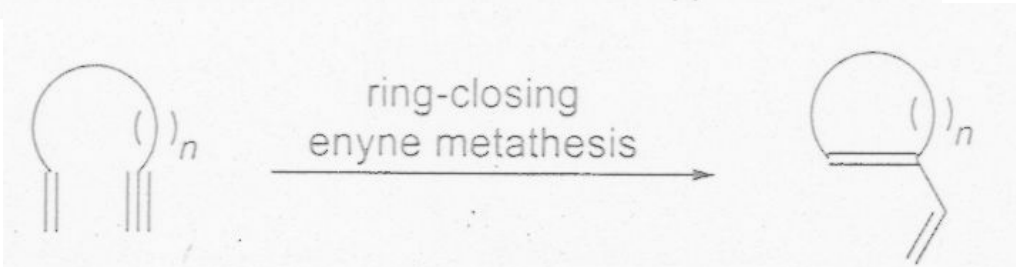

PS - Ru
80°C, 4 h
N
CO2Me
Ts
N
CO2Me
Ts
98%

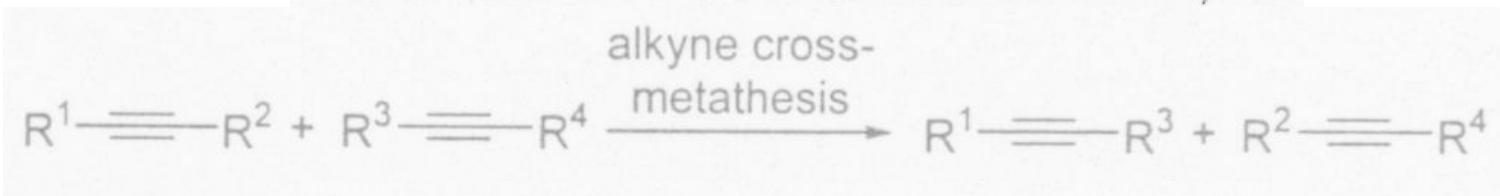
Multiple use of alkene cross-metathesis in the enantioselective total synthesis of bistramide A

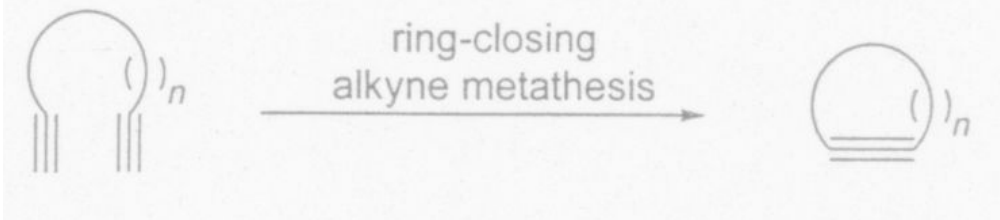
S.Kozmin, JACS 2004, 126, 9546

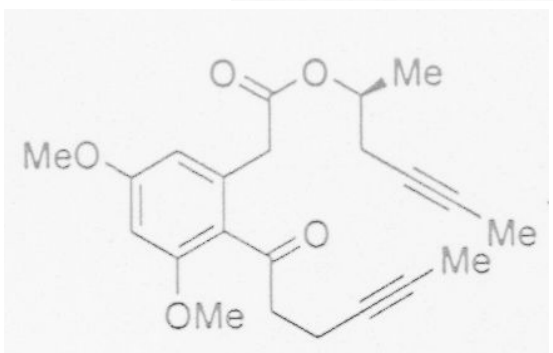

Me
Me
O
O
+
OBn
N
O
O
Me
ring-opening/cross-metathesis cascade
OBn
O
NPhth
Me
+
OBn
OBn
Me
alkene cross-metathesis
OBn
O
OBn
NPhth
+
OBn
Me
Me
H2
oxidation
Me
O
OH
NH
NH
Me
O
O
O
Me
OH
Me
Me
Me
O
bistramide A



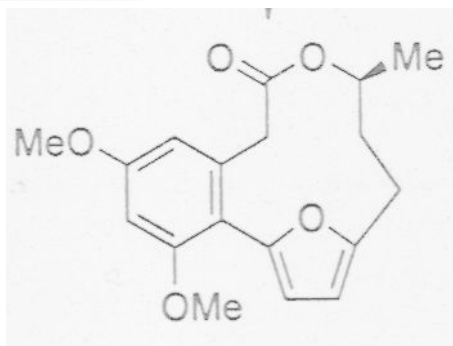








$(tBuO)_3W{\equiv}CMe_3$



(t$^-$)citreoperan


Лауреаты
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ПРЕМИИ


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