Organic Chemistry IV

Organometallic Chemistry for Organic Synthesis

Prof. Paul Knochel

LMU

2013

OCIV

Prüfung:

Freitag 19. Juli 9-11 Uhr

Wieland HS

Wiederholungsklausur:

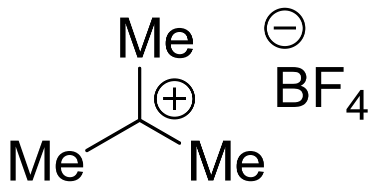
Donnerstag 19. September 14-16 Uhr

Wieland HS

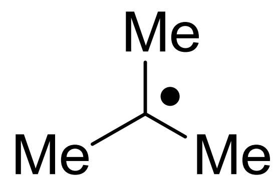
Recommended Literature

1. **F. A. Carey, R. J. Sundberg, Advanced Organic Chemistry**, Fifth Edition Part A and Part B, Springer, 2008, ISBN-13: 978-0-387-68346-1
2. **R. Brückner, Organic Mechanisms**, Springer, 2010, ISBN: 978-3-642-03650-7
3. **L. Kürti, B. Czako, Strategic applications of named reactions in organic synthesis**, Elsevier, 2005, ISBN-13: 978-0-12-429785-2
4. **N. Krause, Metallorganische Chemie**, Spektrum der Wissenschaft, 1996, ISBN: 3-86025-146-5
5. **R. H. Crabtree, The organometallic chemistry of transition metals**, Wiley-Interscience, 2005, ISBN: 0-471-66256-9
6. **M. Schlosser, Organometallics in Synthesis** – A manual, 2nd edition, Wiley, 2002, ISBN: 0-471-98416-7
7. **K. C. Nicolaou, T. Montagnon, Molecules that changed the world**, Wiley-VCH, 2008, ISBN: 978-527-30983-2
8. **J. Hartwig, Organotransition Metal Chemistry: From Bonding to Catalysis**, Palgrave Macmillan, 2009, ISBN-13: 978-1891389535
9. **P. Knochel, Handbook of Functionalized Organometallics**, Volume 1 und 2, Wiley-VCH, 2005, ISBN-13: 978-3-527-31131-6

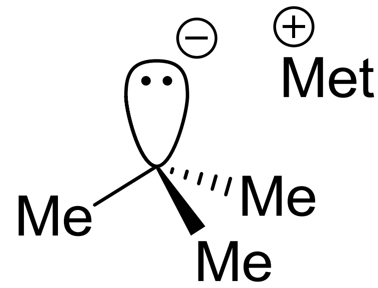
Importance of organometallics



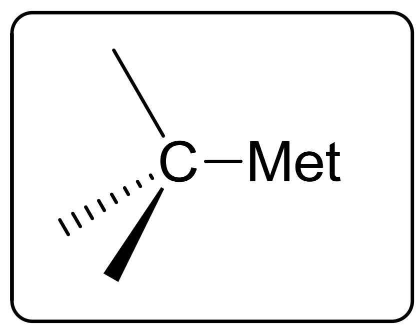
carbenium ion



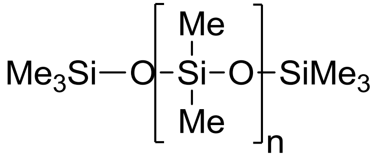
radical



organometallic reagent

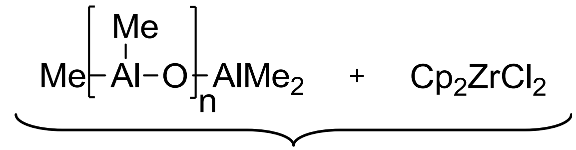


Industrial production



Silicone

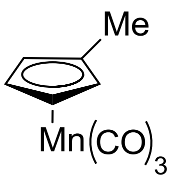
Et_4Pb



Kaminsky catalyst
n=5-20   syndiotacticity of polypropylene

BuLi

$[Bu_3Sn]_2O$



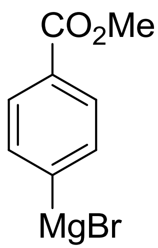
Industrial annual production of various organometallics

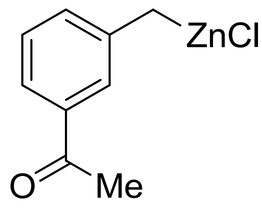
Organometallic	production [T / year]
Si	700 000
Pb	600 000
Al	50 000
Sn	35 000
Li	900

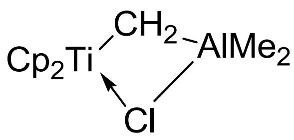
Organometallic reagents and catalysts for the organic synthesis

organometallic reagents:

BuLi







Tebbe reagent

H(Cl)ZrCp$_2$

Schwarz reagent

organometallic catalysts:

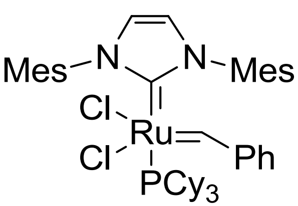
Pd(PPh$_3$)$_4$

CpCo(CO)$_2$

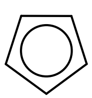
[RhCl(CO)$_2$]$_2$

ClRh(PPh$_3$)$_3$

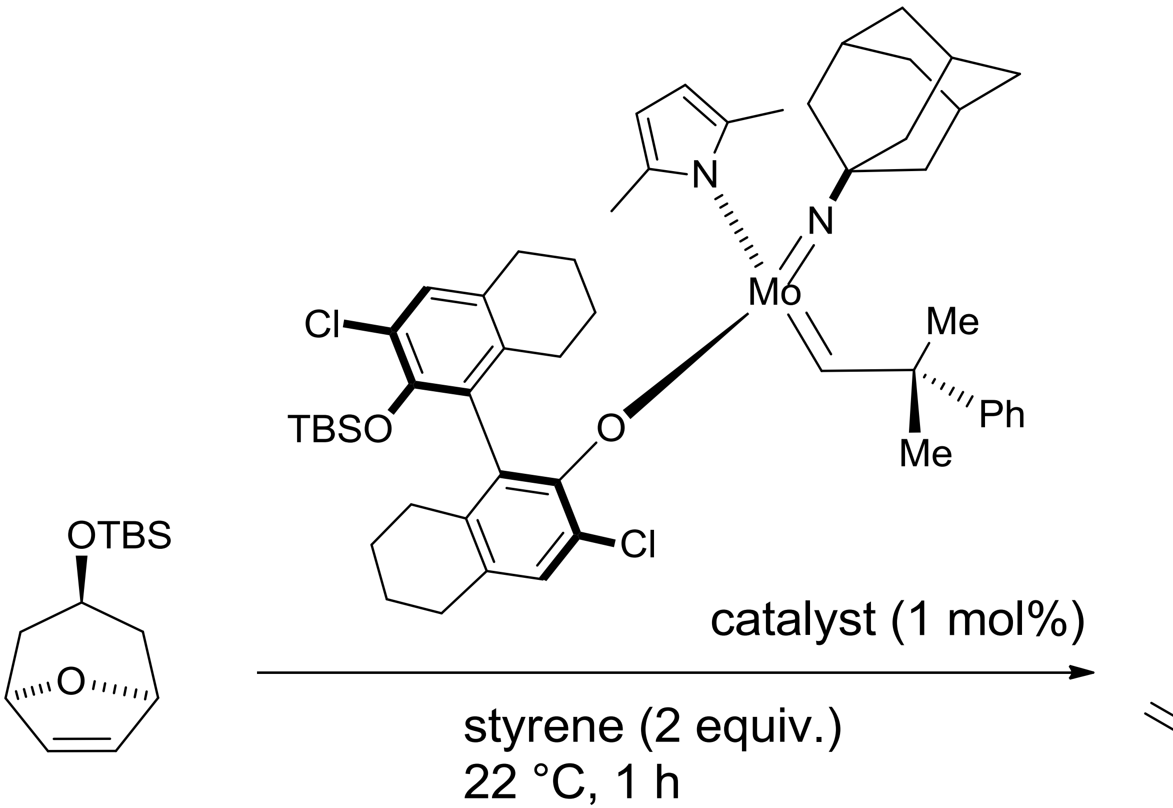
Wilkinson's catalyst

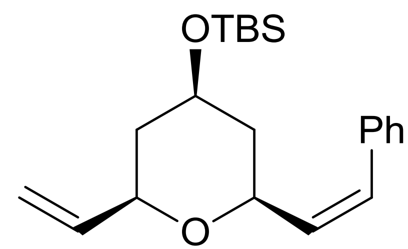


Grubbs II catalyst

 ≡ Cp

State of the art

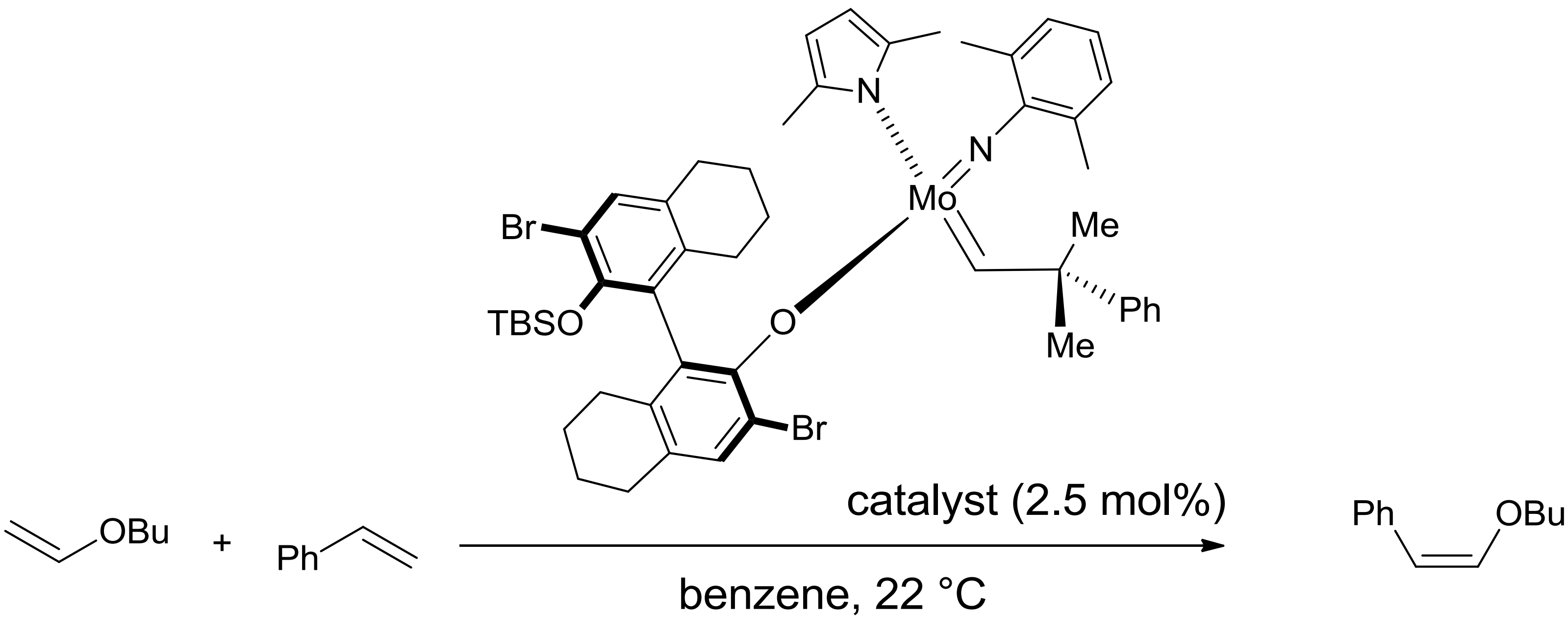




80%; dr: 95 : 5
Z:E > 98:2

A. H. Hoveyda, *J. Am. Chem. Soc*. **2009**, *131*, 3844
O. Eisenstein, C. Copéret *J. Am. Chem. Soc*. **2007**, *129*, 8207

State of the art

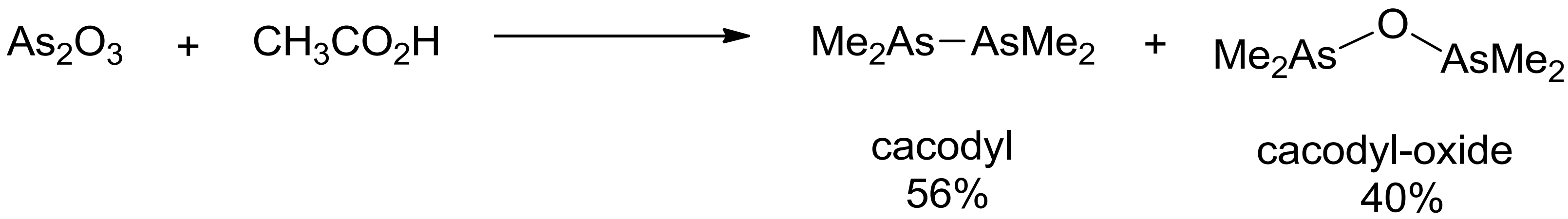


73%; Z:E > 98:2

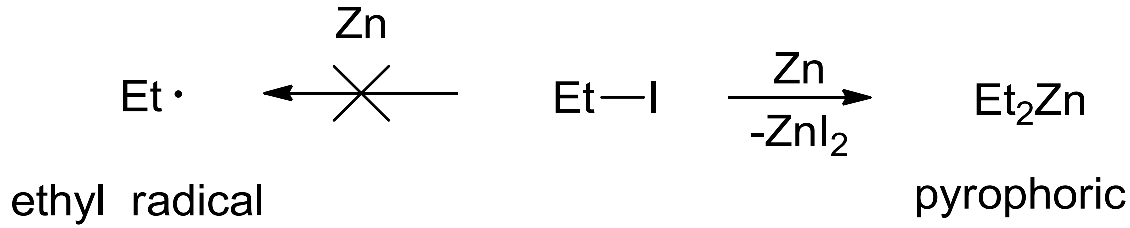
A. H. Hoveyda, *Nature* **2011**, *471*, 461
A. H. Hoveyda, *Nature* **2008**, *456*, 933

Historic point of view

1757 - Louis Cadet de Gassicourt (parisian apothecary)



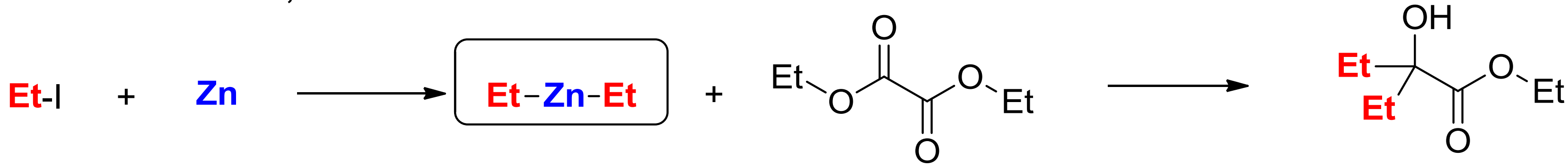
E. Frankland (1848), University of Marburg, initial goal: synthesis of an ethyl radical



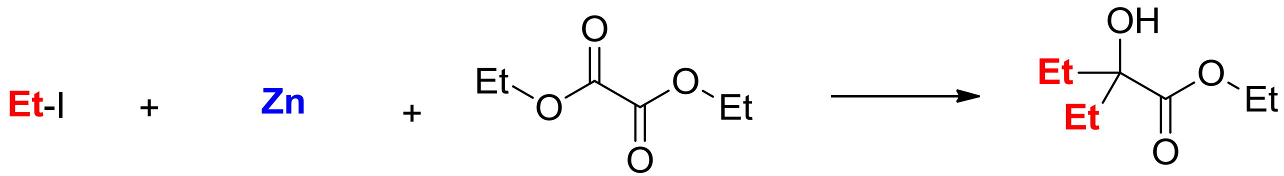
Universität Marburg (1848)

Organometallic chemistry of the XIX century

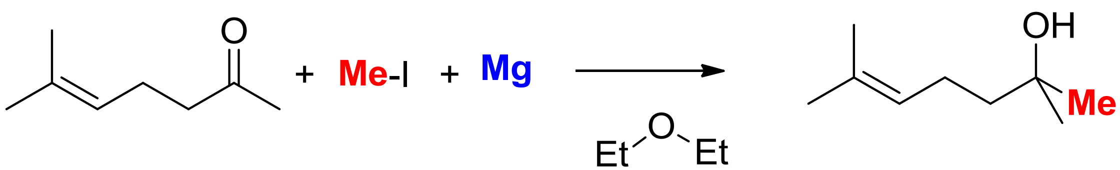
Frankland **1848**, **1863**



Beilstein **1862,** Saytzeff **1870,** Wagner **1875**



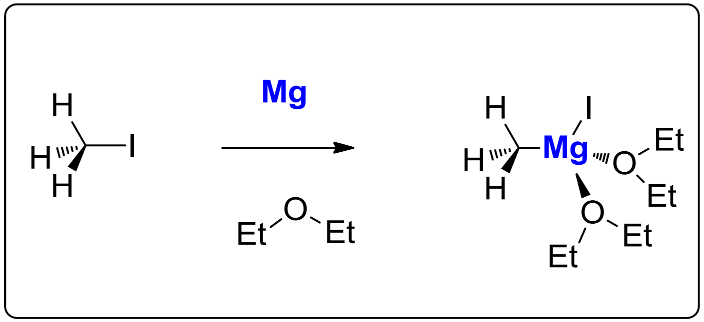
Barbier **1899**

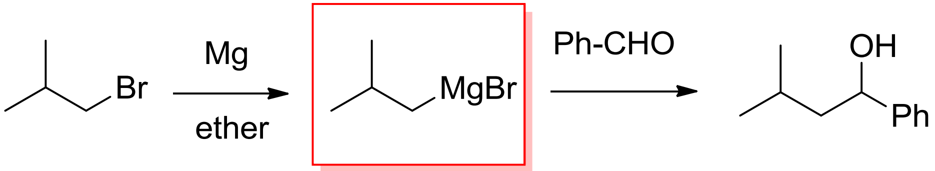


Ph. Barbier *Comptes Rendus de l'Académie des Sciences*, **1899**, *128*, 110

Organometallic chemistry of the XIX century

Pl. X. *Victor Grignard dans son laboratoire de Nancy*
1912



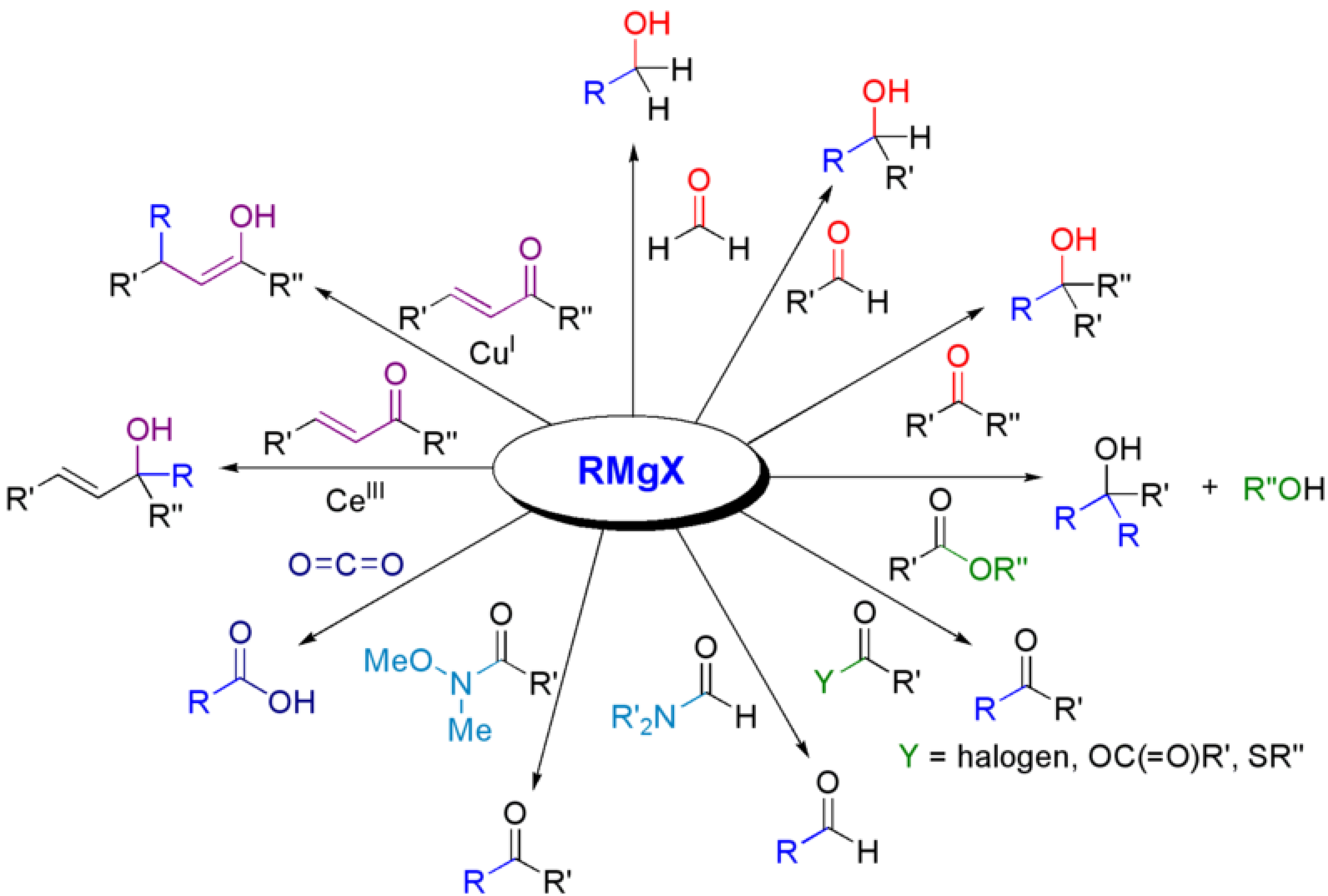


reactif de Grignard

V. Grignard

Comptes Rendus de l'Académie des Sciences, **1900**, *130*, 1322

Reactivity of the Grignard reagents



Historic point of view

Victor Grignard (1900)

$$Et{-}Br \xrightarrow[\text{ether, 40 °C}]{Mg} Et{-}MgBr$$

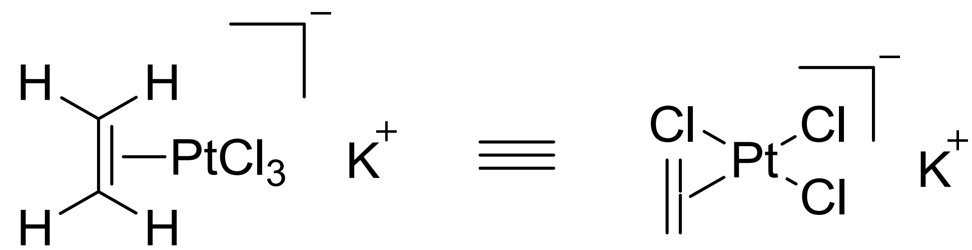
Karl Ziegler (1919)

$$BuCl \quad + \quad 2Li \xrightarrow[\text{under Argon}]{\text{pentane}} BuLi \quad + \quad LiCl$$

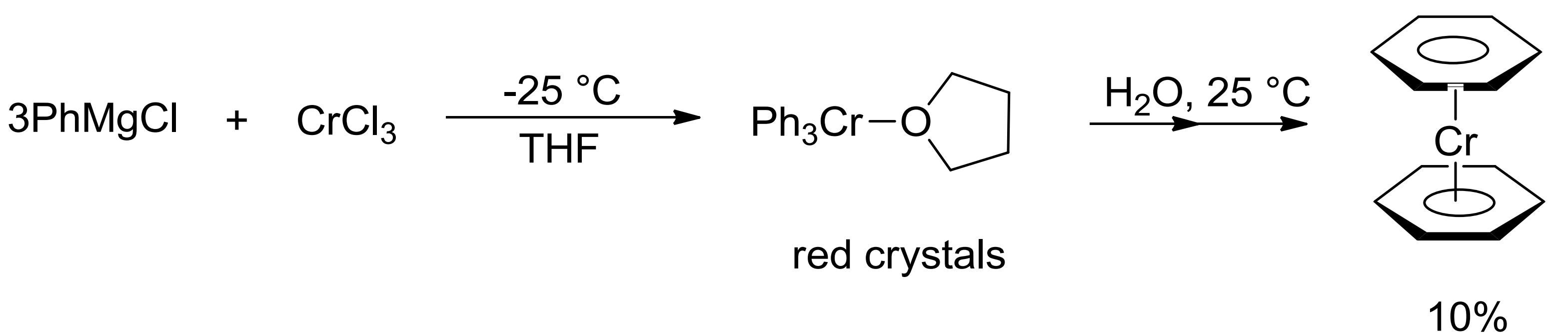
Historic point of view

first transition metal organometallics:

Zeise's Salz (1827)



Hein (1919)

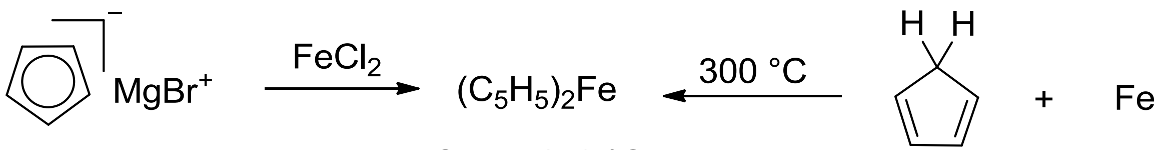


Historic point of view

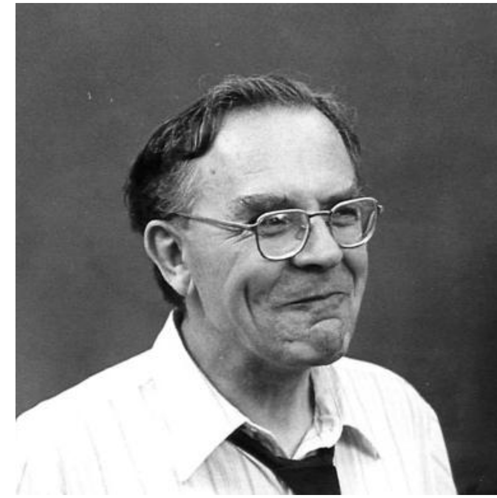
1951 : synthesis of ferrocene

Pauson (Scotland) 7. August 1951

Miller 11. June 1951

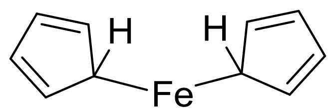


Smp.: 172 °C

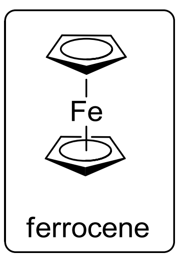


G. Wilkinson

1952
structural proposal by Pauson

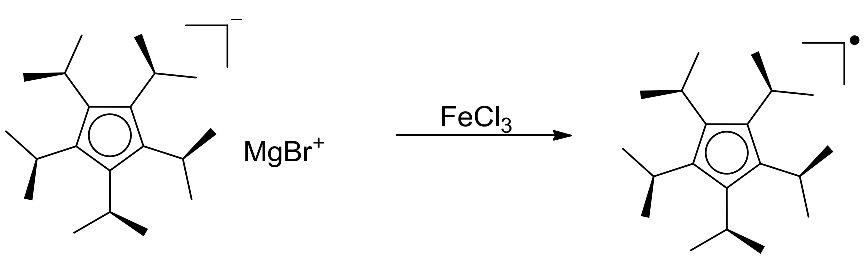


correct structure by G. Wilkinson and R. B. Woodward



G. Wilkinson, R. B. Woodward *J. Am. Chem. Soc.* **1952**, *74*, 2125
R.B. Woodward *J. Am. Chem. Soc.* **1952**, *74*, 3458

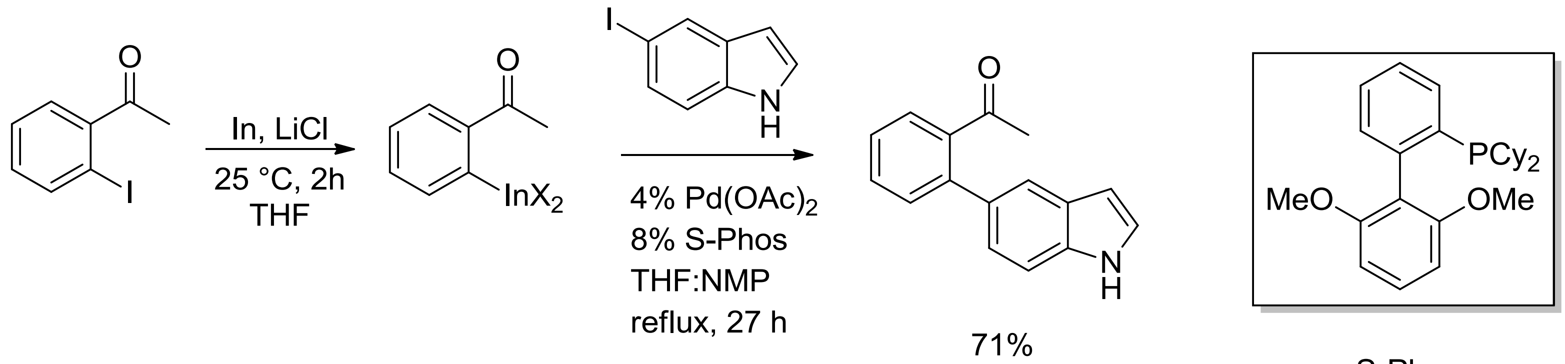
R. B. Woodward



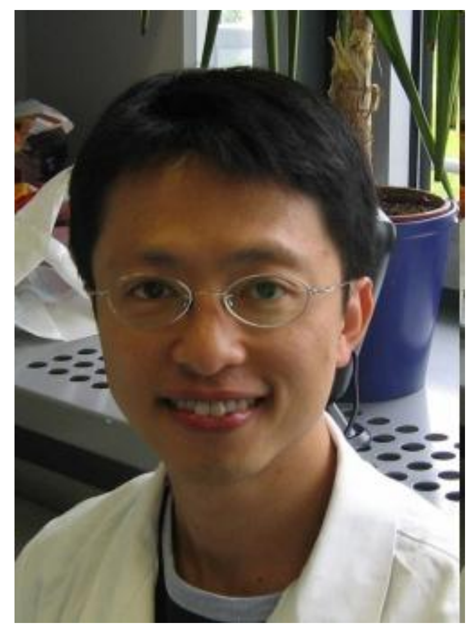
H. Sitzmann *J. Am. Chem. Soc.* **1993**, *115*, 12003 radical formation

Goal of the lecture

main goal of this course: applications of organometallic compounds in modern organic synthesis



S-Phos

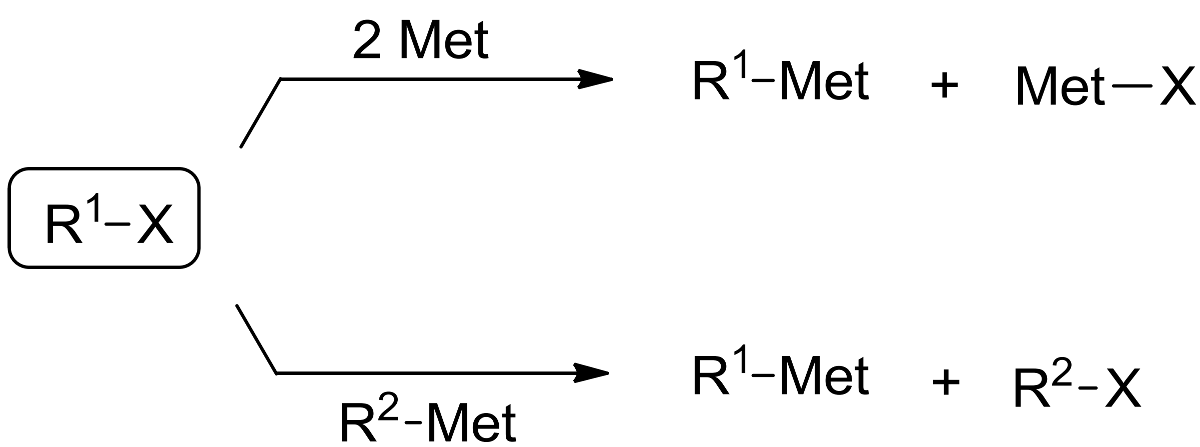


Y.-H. Chen, *Angew. Chem. Int. Ed*. **2008**, *47*, 7648.

General synthetic methods for preparing organometallic reagents

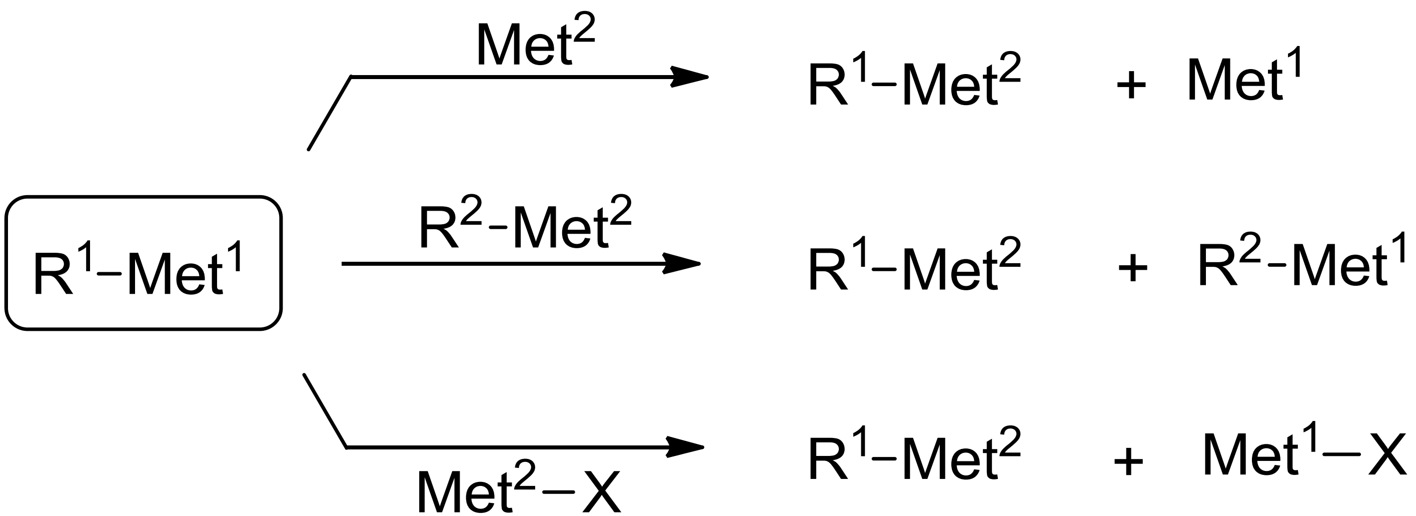
classification according to starting materials

direct synthesis *via* an oxidative addition and halogen-metal exchange



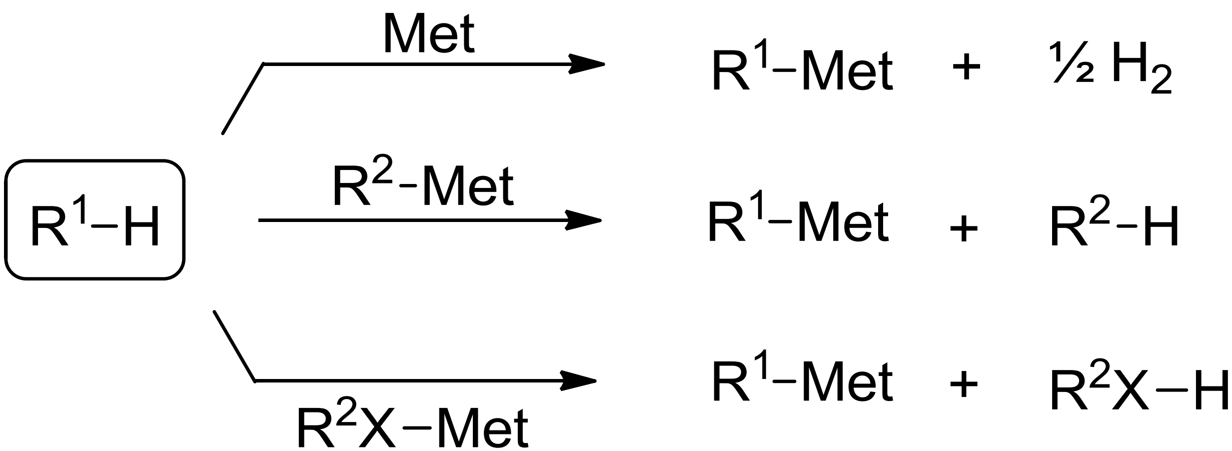
Classification according to starting materials

transmetalation



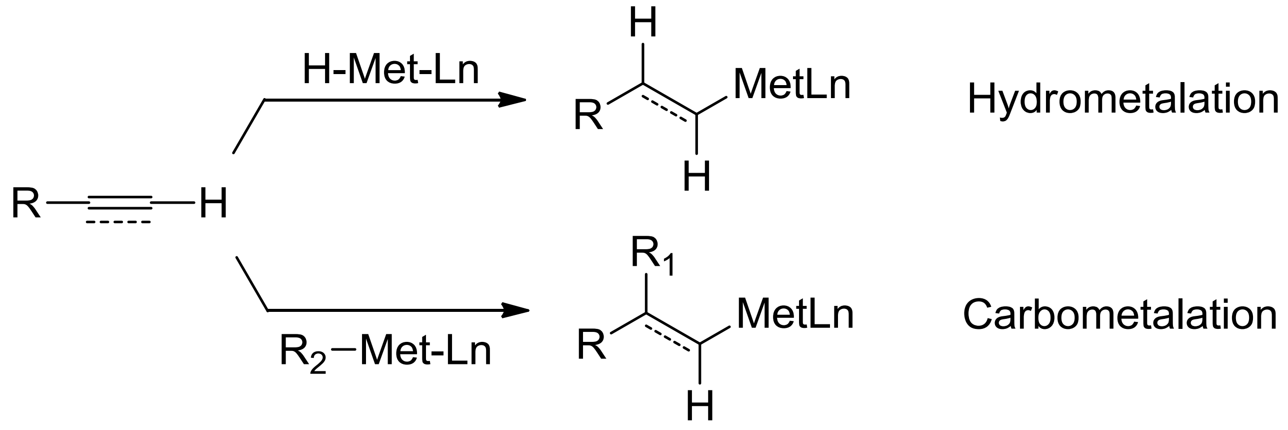
Classification according to starting materials

metalation



Classification according to starting materials

carbometalation and hydrometalation



Synthesis starting from organic halides

direct synthesis - oxidative addition

$$R-X \quad + \quad 2Met \longrightarrow \boxed{R-Met} \quad + \quad Met-X$$

driving force of the reaction:

$$\Delta H = \Delta H[Met-X] + \Delta H[C-Met] - \Delta H[C-X] - \text{lattice energy}$$

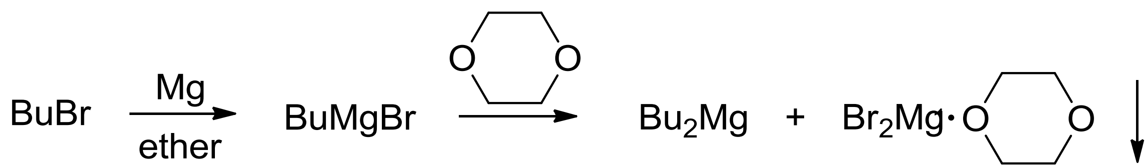
$$4\ EtCl + 3\ Pb \longrightarrow Et_4Pb + 2\ PbCl_2 \quad \text{endothermic}$$

$$4\ NaPb + 4\ EtCl \longrightarrow Et_4Pb + 3\ Pb + 3\ NaCl \quad \text{exothermic}$$

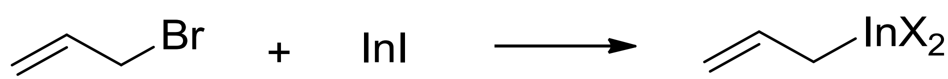
Direct Synthesis - Oxidative Addition

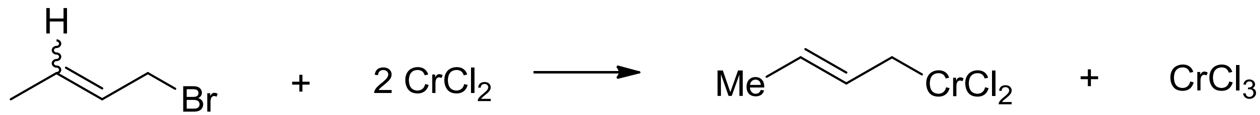
examples:

$$BuCl \xrightarrow{2\ Li} BuLi + LiCl$$



$$PbI_2 + MeI \longrightarrow MePbI_3$$





E/Z-mixture

pure E-isomer

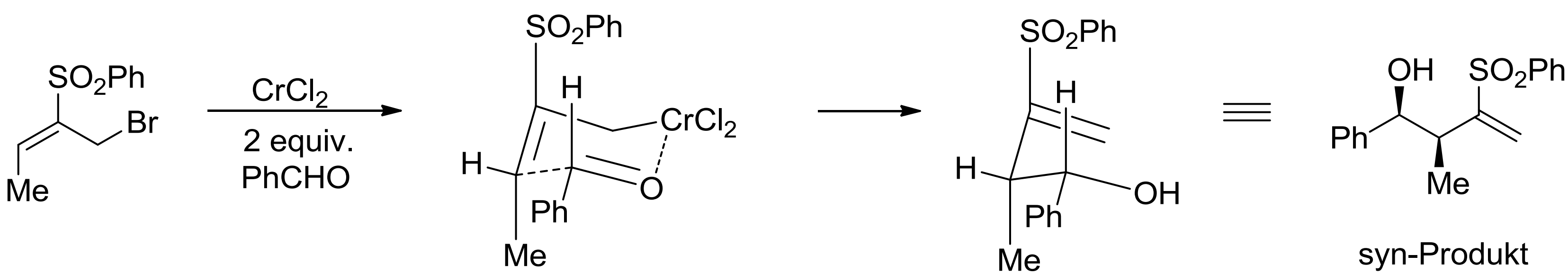
Direct Synthesis - Oxidative Addition

mechanism:

$$\text{R-Br} + \dot{\text{Cr}}\text{Cl}_2 \longrightarrow \text{R}\cdot + \text{BrCrCl}_2$$

$$\text{R}\cdot + \dot{\text{Cr}}\text{Cl}_2 \longrightarrow \text{RCrCl}_2$$

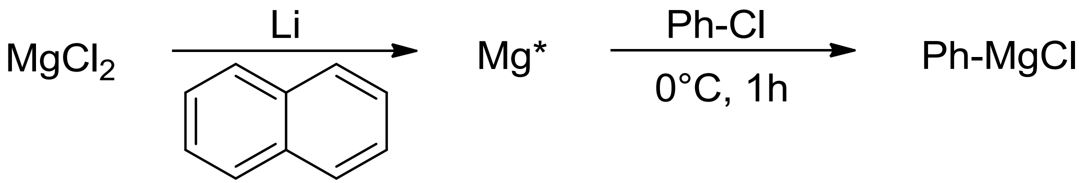
$$\text{R-Br} + 2\,\dot{\text{Cr}}\text{Cl}_2 \longrightarrow \text{RCrX}_2 + \text{CrX}_3$$

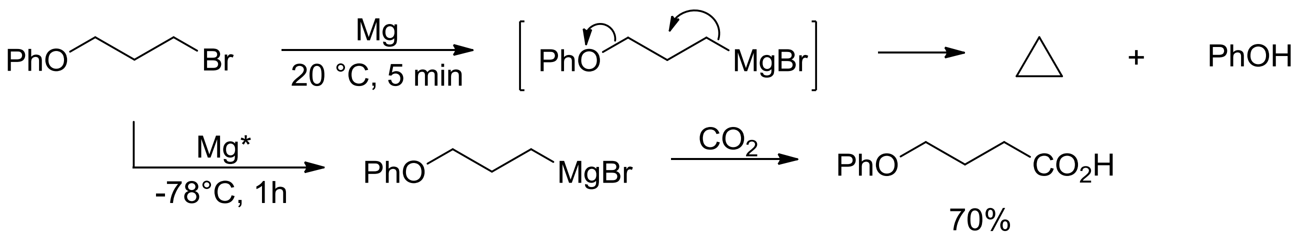


P. Knochel *Tetrahedron Lett*. **1986**, *27*, 5091

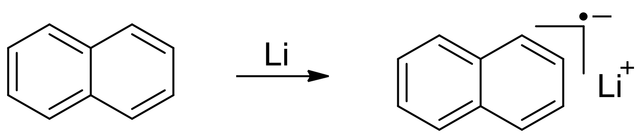
Activation of the metal: the *Rieke*-approach

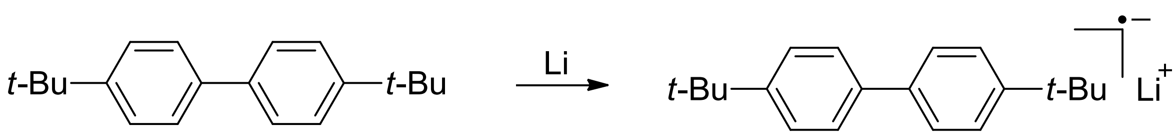
activation of the metal: R. D. Rieke, *Science* **1989**, *246*, 1260





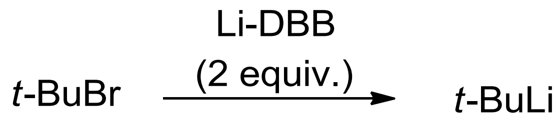
Activation of lithium: formation of soluble Li-sources:

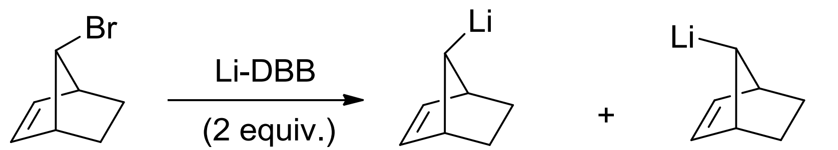




P.P. Freeman, L.L. Hutchinson *J. Org. Chem*. **1983**, *48*, 4705

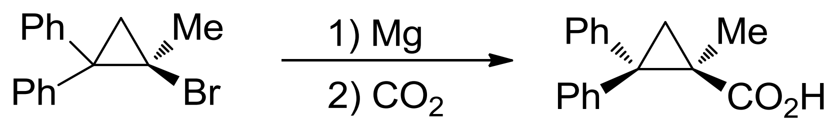
Mechanism of the metal insertion





80 : 20

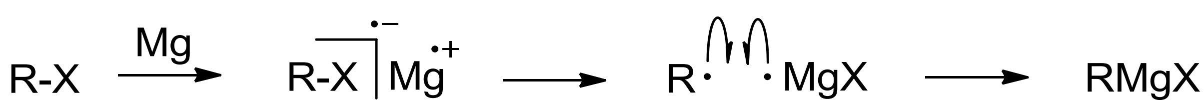
loss stereochemical information



90% ee

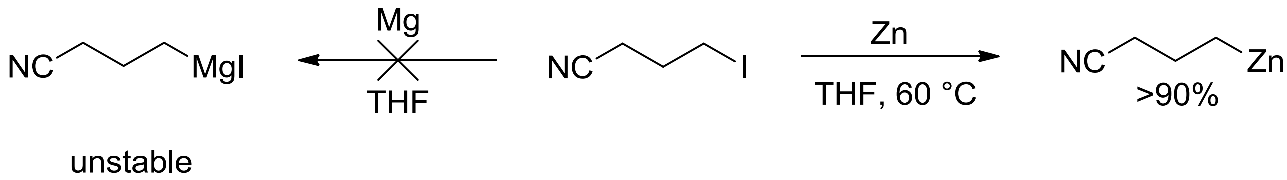
12% ee

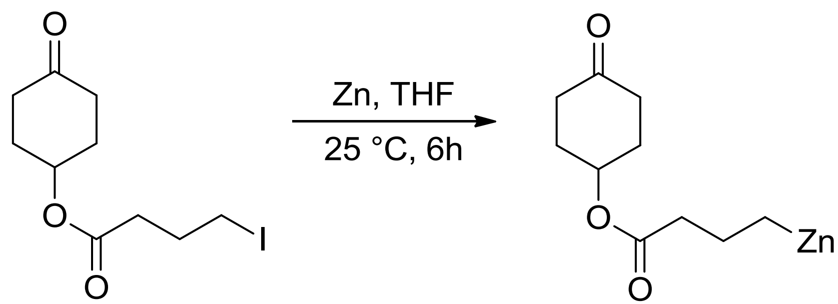
H.M. Walborsky: *J. Am. Chem. Soc*. **1989**, *11*, 1896



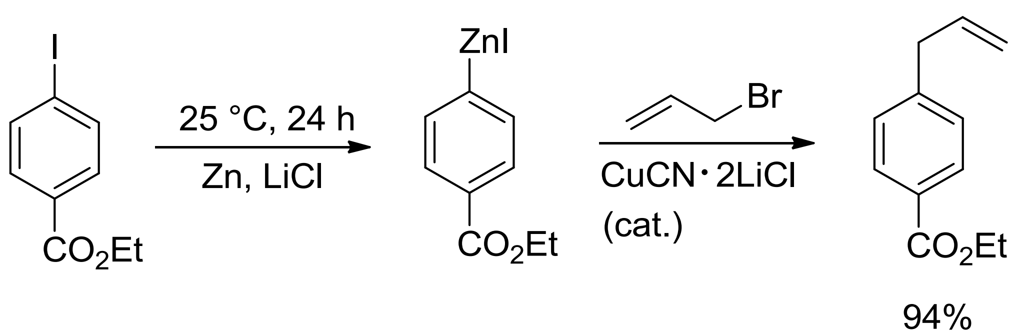
radical mechanism

Preparation of functionalized organometallics



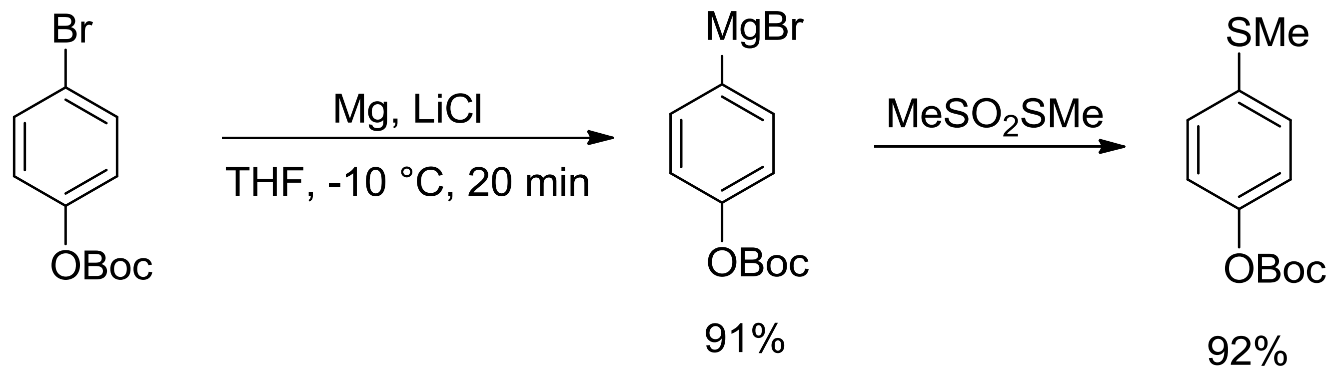


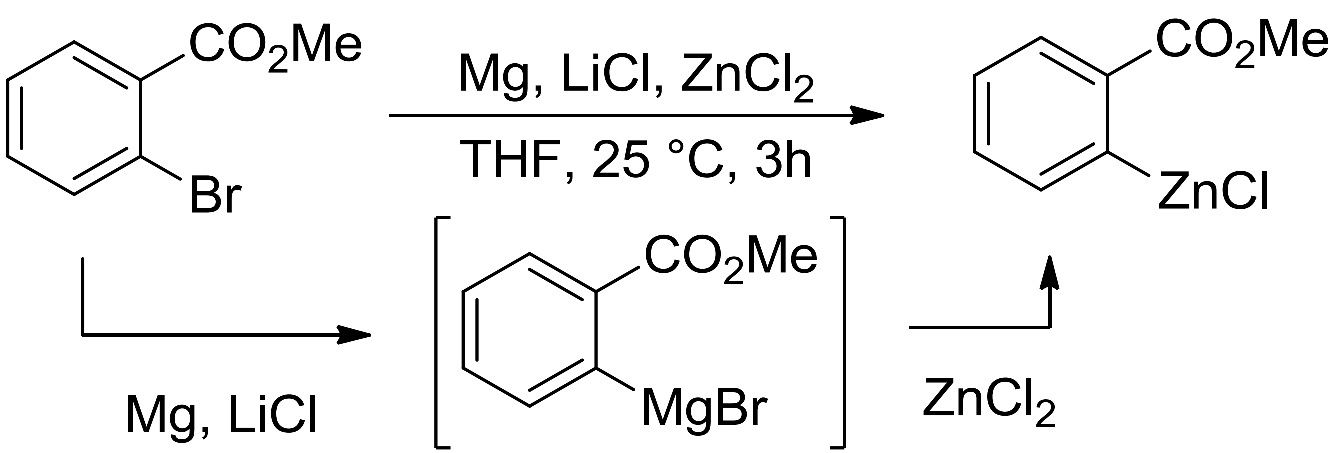
P. Knochel, *J. Org. Chem*. **1988**, *53*, 2390
P. Knochel, *Org. React*. **2001**, *58*, 417.



A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem. Int. Ed*. **2006**, *45*, 6040.

Preparation of functionalized organometallics

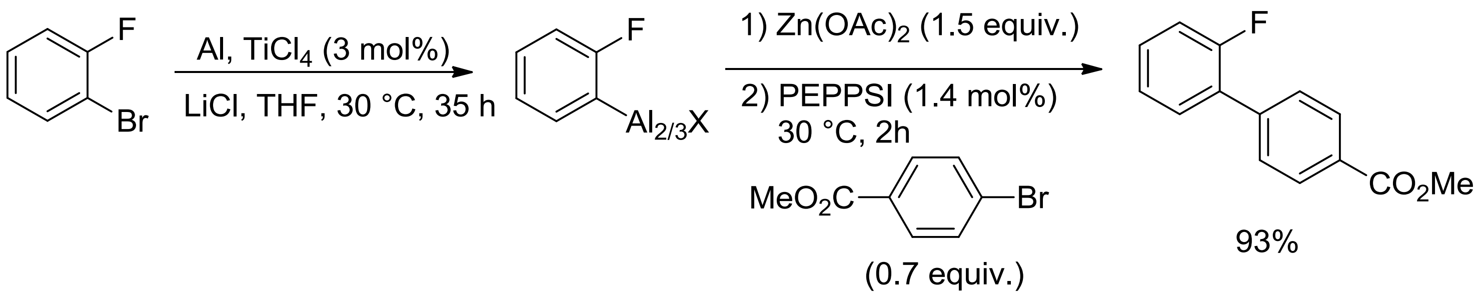




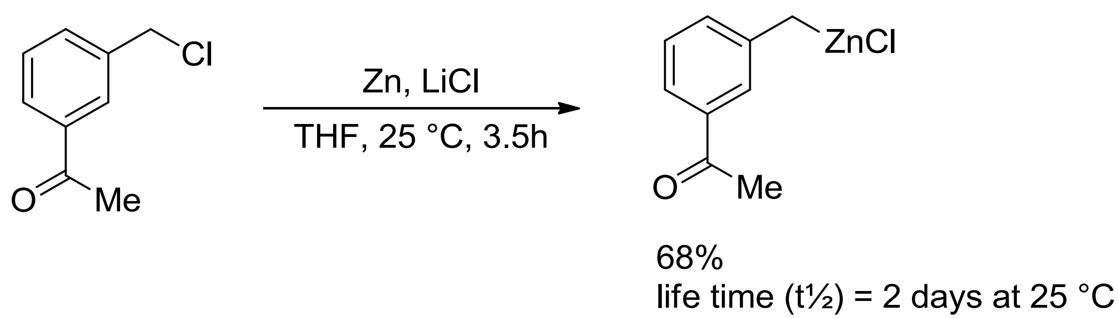
F. Piller, P. Knochel *Chem. Eur. J*. **2009**, *15*, 7192

Preparation of functionalized organometallics

activation of Al using LiCl and $TiCl_4$, $BiCl_3$, $PbCl_2$ or $InCl_3$

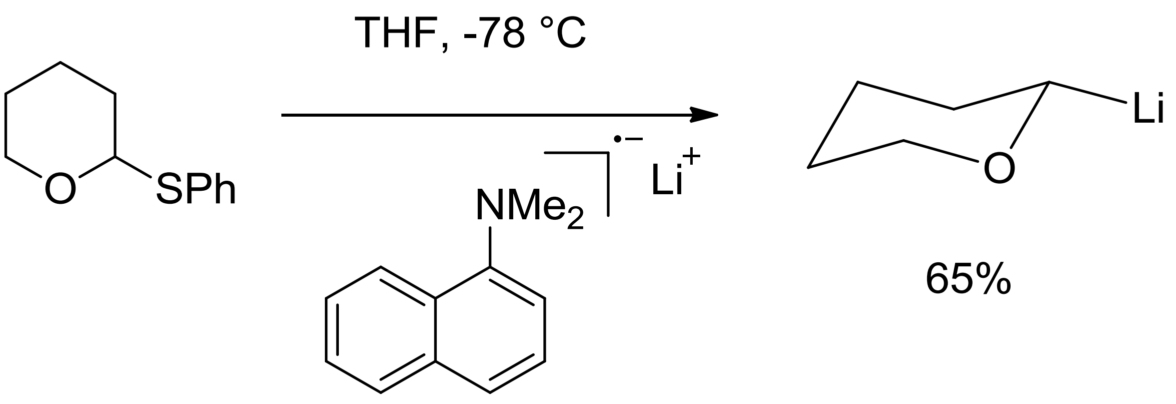


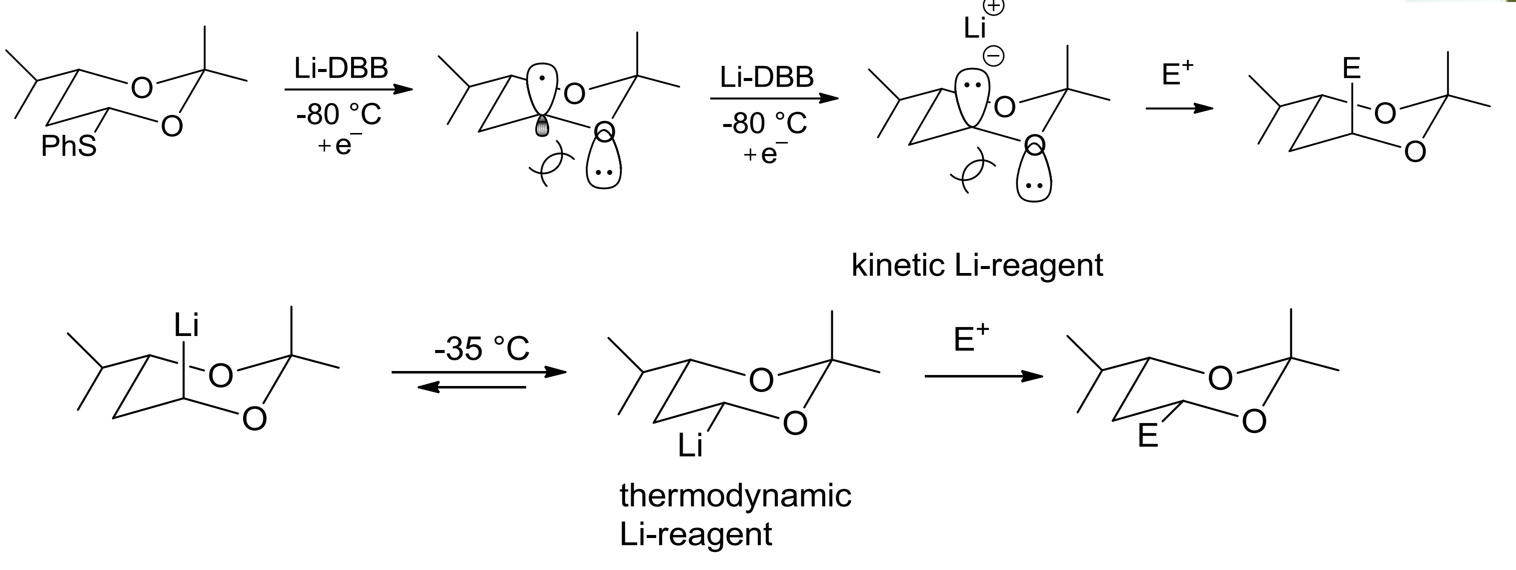
T. Blümke, Y.-H. Chen, P. Knochel *Nature Chemistry*, **2010**, *2*, 313



A. Metzger, P. Knochel *Org. Lett*. **2008**, *10*, 1107

Extension to insertion reactions to C-S bonds



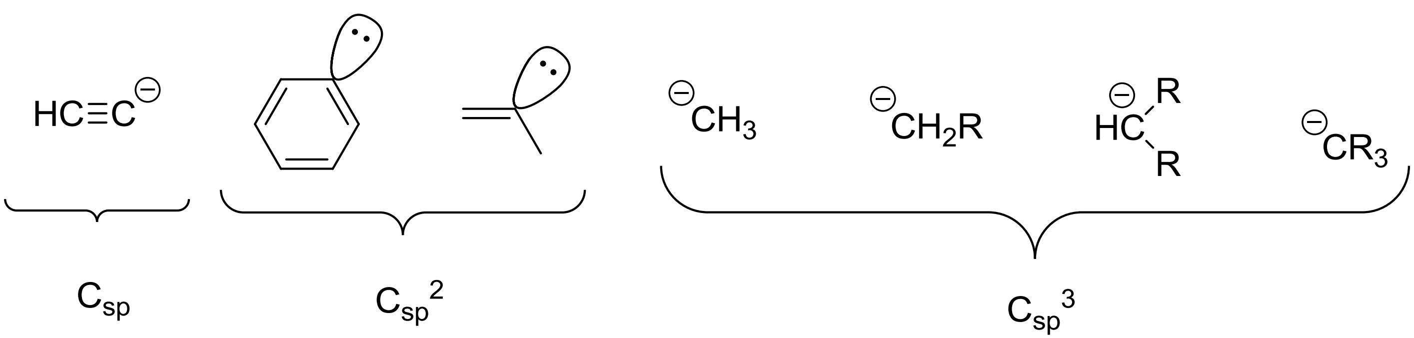


S. Rychnosvsky *J. Org. Chem*. **1989**, *54*, 4982; *J. Org. Chem*. **1990**, *95*, 5550

The Halogen-Metal-Exchange

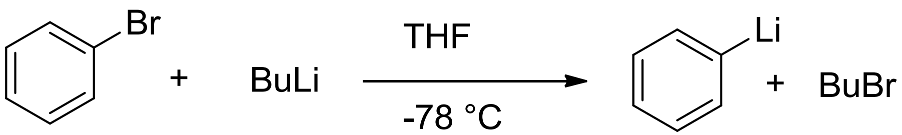
$$R^1{-}X + R^2{-}Met \rightleftharpoons R^2{-}X + \boxed{R^1{-}Met}$$

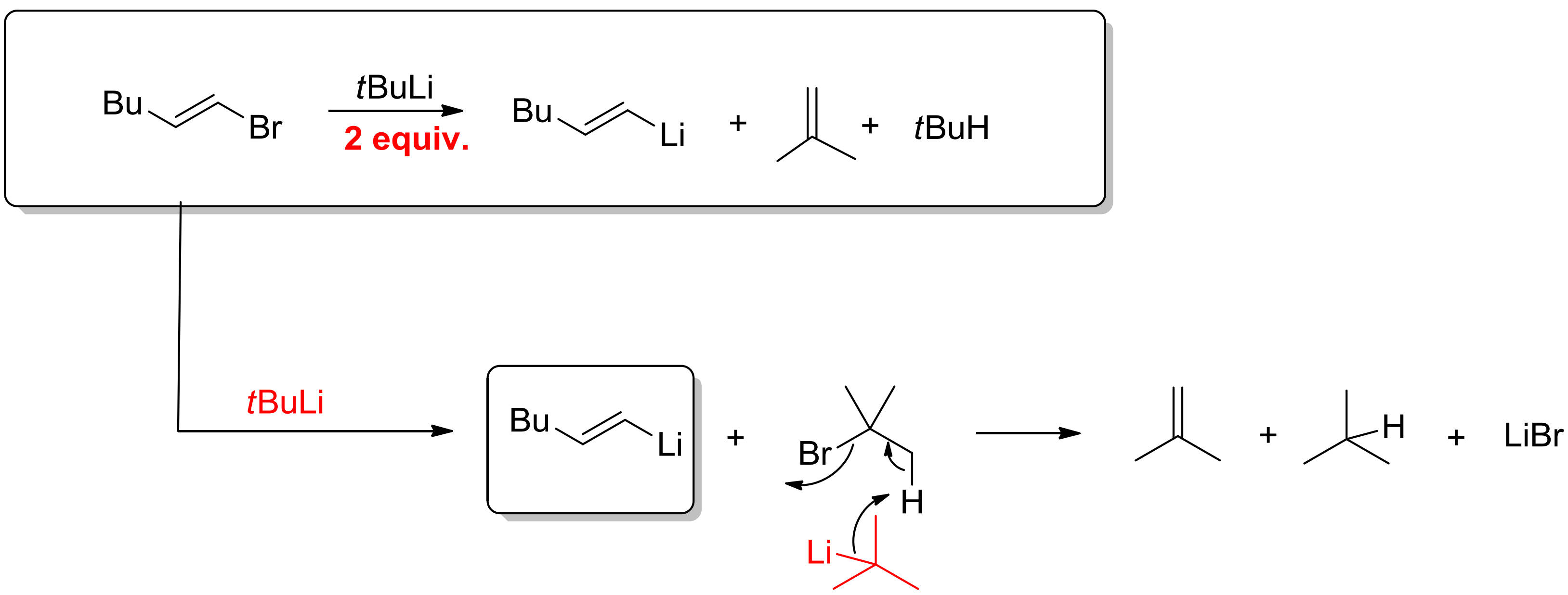
driving force: the most stable carbanion is always formed

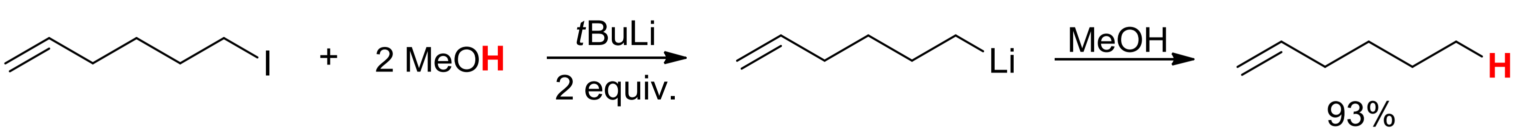


The Halogen-Metal-Exchange

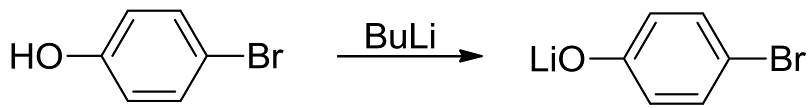
1939: the Wittig-Gilman reaction







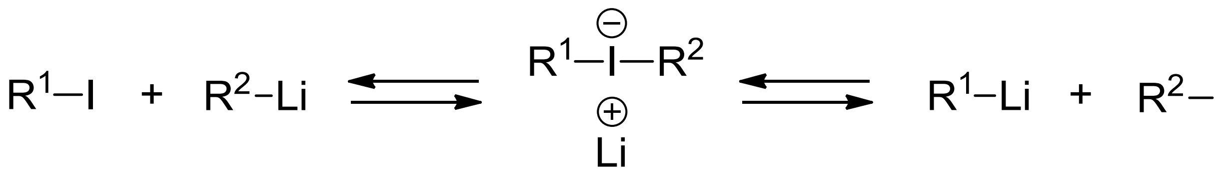
The Halogen-Metal-Exchange

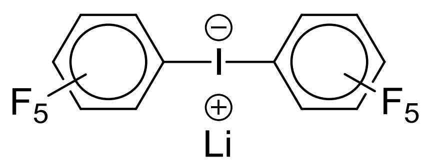


I >> Br >> Cl

rate of the halogen/metal exchange

mechanism:

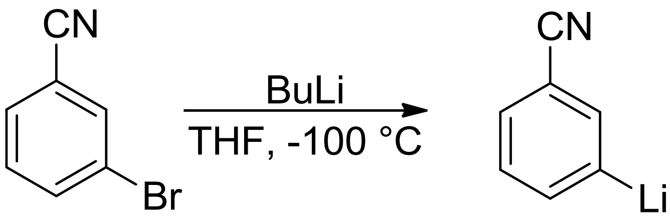




has been isolated

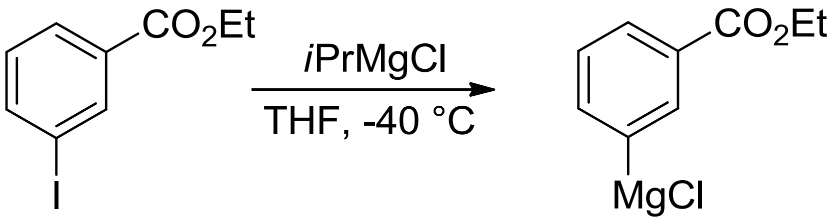
H. J. Reich, A. W. Sanders, A. T. Fiedler, M. J. Bevan *J. Am. Chem. Soc*. **2002**, *124*, 13386

The Halogen-Metal-Exchange : tolerance of functional groups



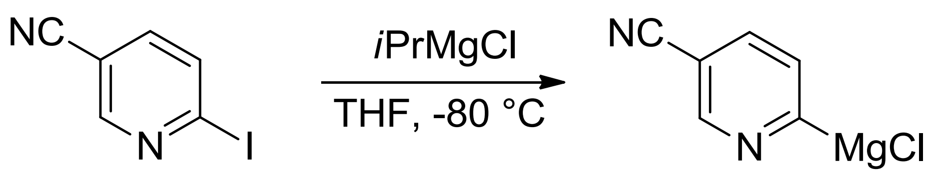
Stable only at -100 °C

W. E. Parham, L. D. Jones, Y. Sayed J. Org. Chem. 1975, 40, 2394



> 90 %

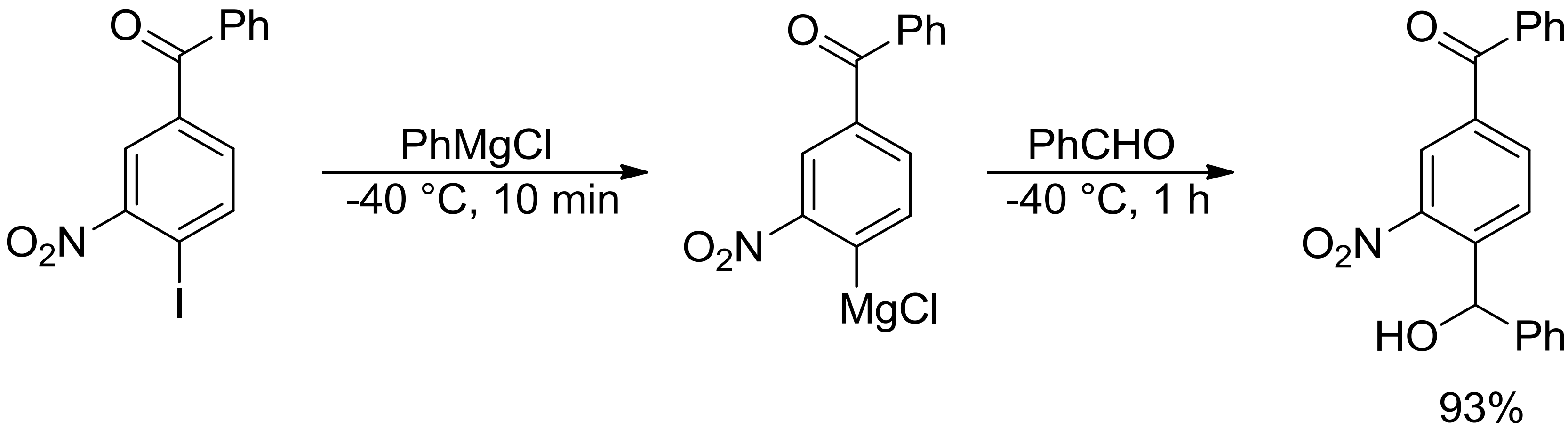
M. Rottländer, P. Knochel, Angew. Chem. Int. Ed. 1998, 40, 1801



> 90 %

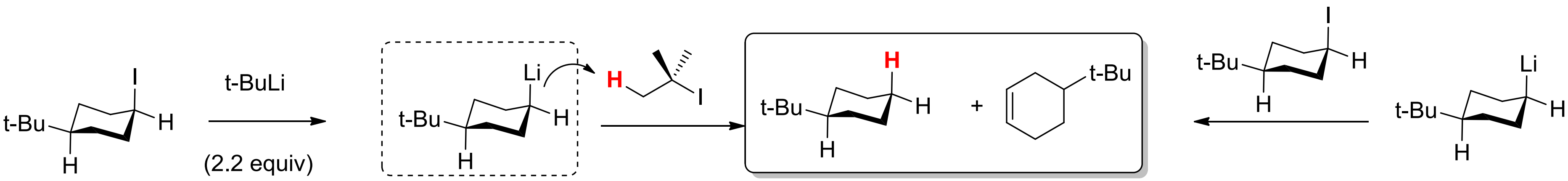
H. Ren, P. Knochel, Chem.Comm. **2006**, 726

The iodine- magnesium-exchange: compatibility with a nitro group



I. Sapountzis, P. Knochel *Angew. Chem. Int. Ed*. **2003**, *42*, 4438

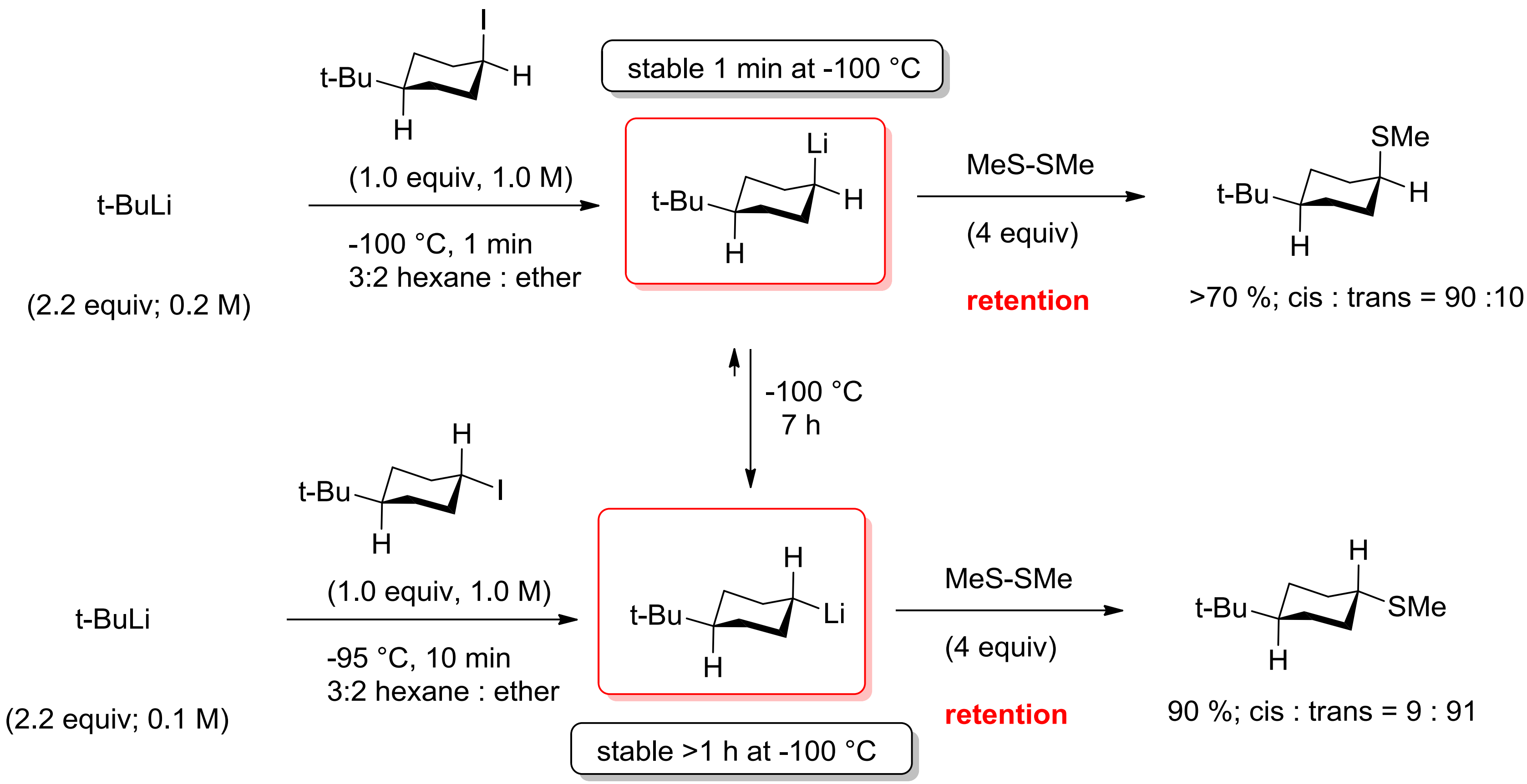
A secondary iodine/lithium exchange on cyclohexyl iodides



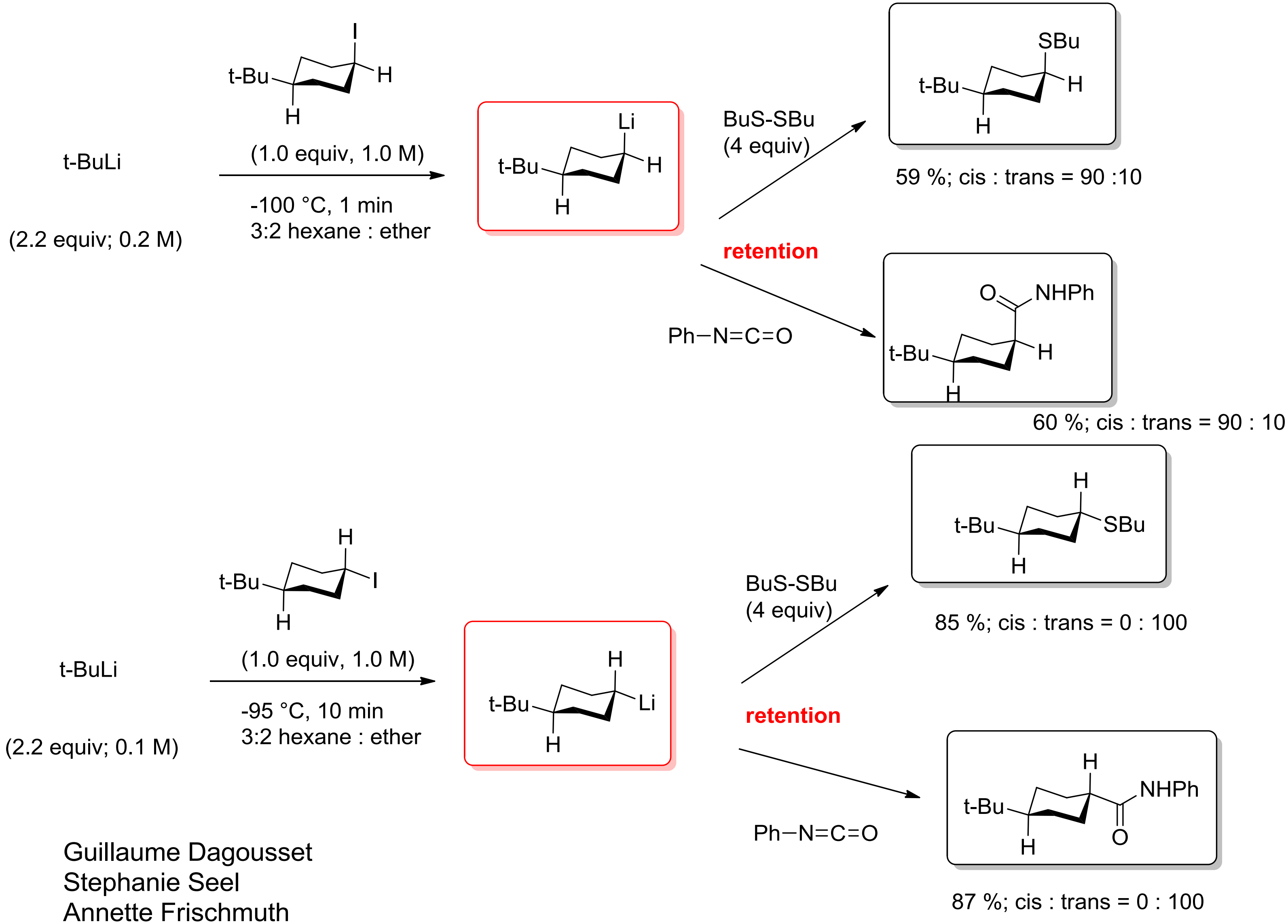
see W.F. Bailey, J.D. Brubaker, K.P. Jordan, *J. Organomet. Chem.* **2003**, *681*, 210

Stephanie SEEL

A secondary iodine/lithium exchange on cyclohexyl iodides

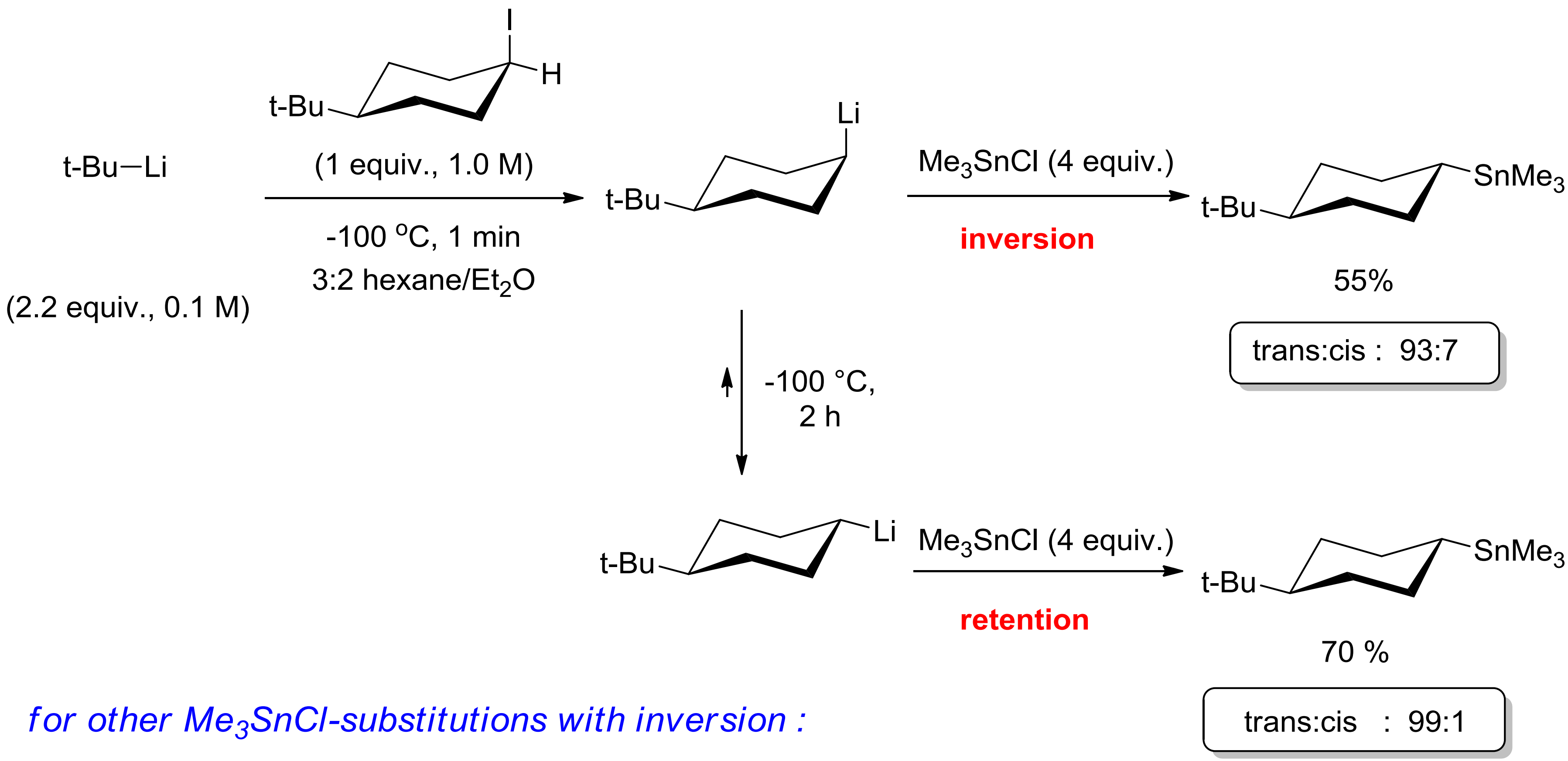


A secondary iodine/lithium exchange on cyclohexyl iodides



Guillaume Dagousset
Stephanie Seel
Annette Frischmuth

Quenching with Me_3SnCl with inversion



for other Me_3SnCl-substitutions with inversion :

D. Hoppe *Angew.Chem.Int.Ed.Engl.* **1990**, *29*, 1424; *Chem. Eur. J.* **2001**, *7*, 423

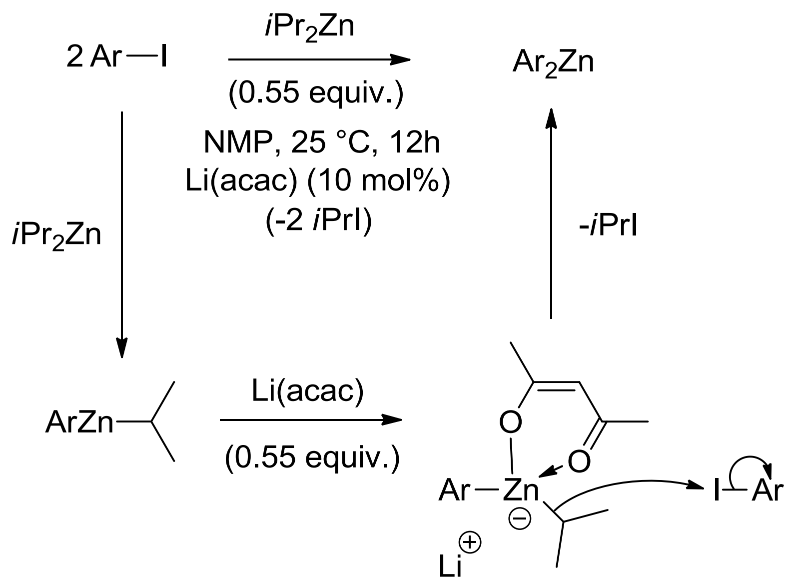
J. Clayden *Tetrahedron Lett.* **1992**, *38*, 2568;

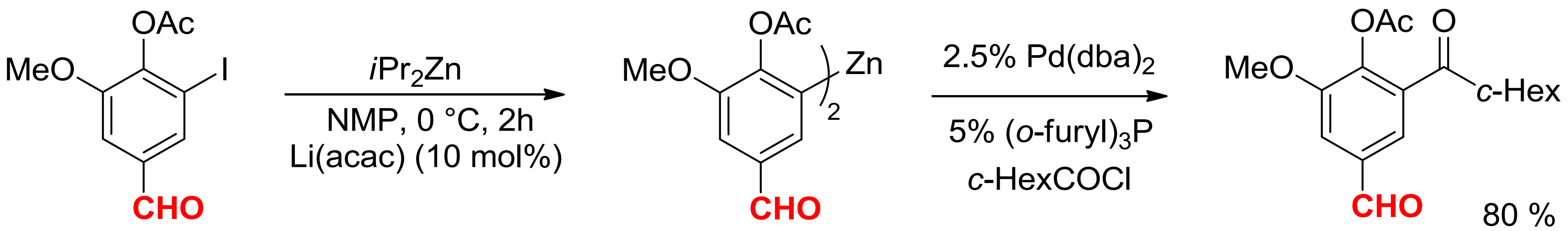
P. Beak, *J. Am. Chem. Soc.* **1997**, *119*, 11561;

R. E. Gawley, *J. Am. Chem. Soc.* **2000**, *122*, 3344.

The iodine/zinc-exchange

catalysis of the halogen-metal exchange

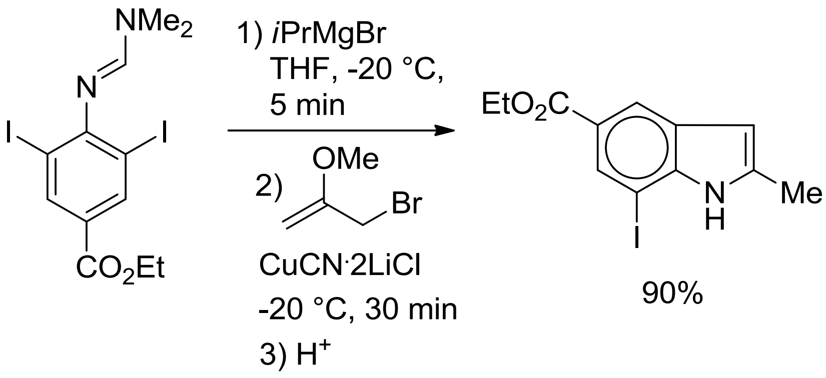




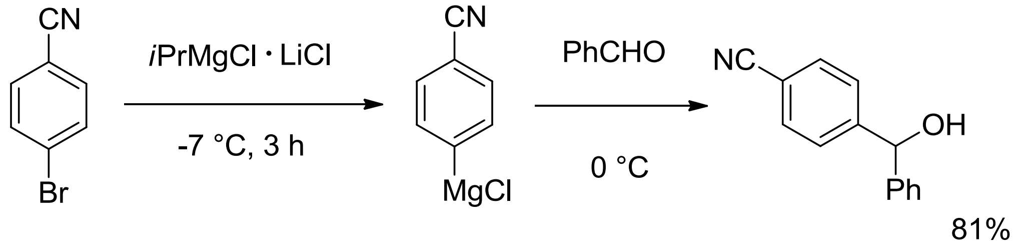
F. Kneisel, P. Knochel *Angew. Chem. Int. Ed*. **2004**, *43*, 1017

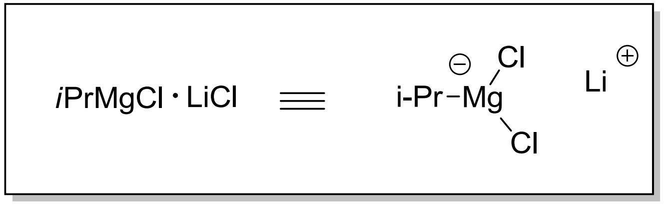
The Halogen-Metal-Exchange

indole-synthesis



D. M. Lindsay, W. Dohle, A. E. Jensen, F. Kopp, P. Knochel *Org. Lett.*, **2002**, *4* , 1819



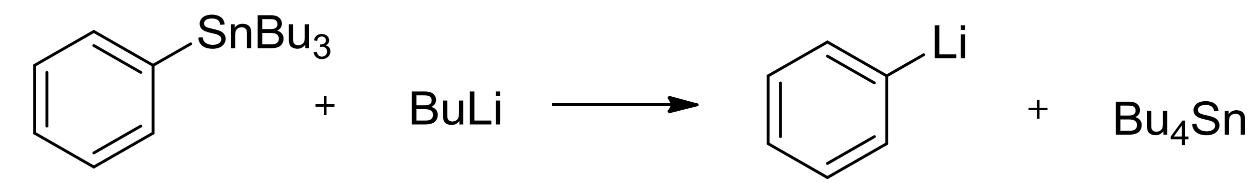


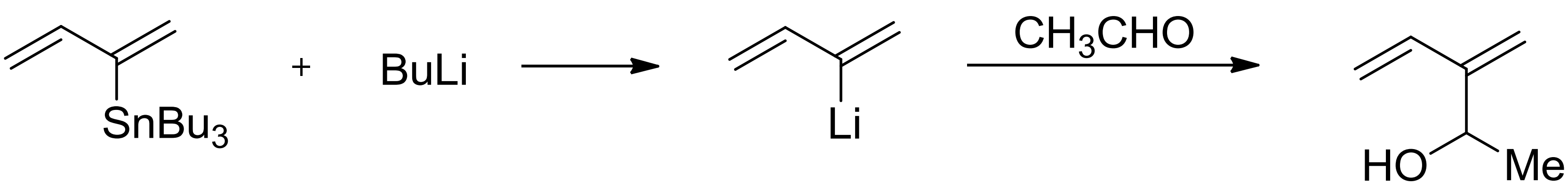
A. Krasovskiy, P. Knochel *Angew. Chem. Int. Ed.* **2004**, *43*, 3333

Transmetalation

a) $$R^1\text{–}Met^1 + R^2\text{–}Met^2 \rightleftharpoons R^1\text{–}Met^2 + R^2\text{–}Met^1$$

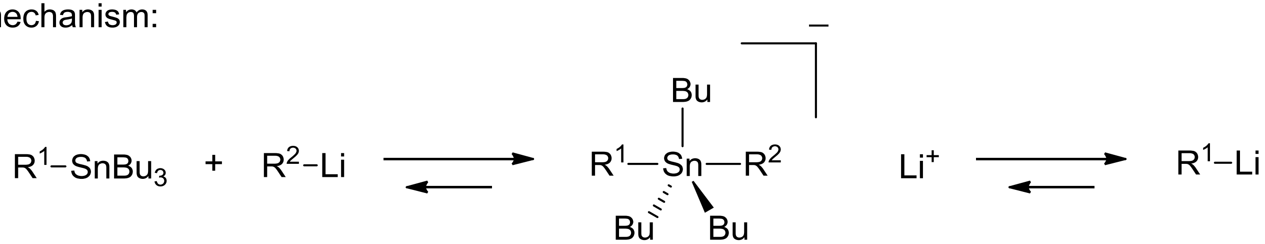
the most stable carbanion is linked to the most electropositive metal



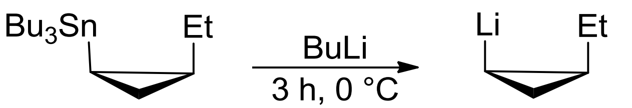


Transmetalation

mechanism:



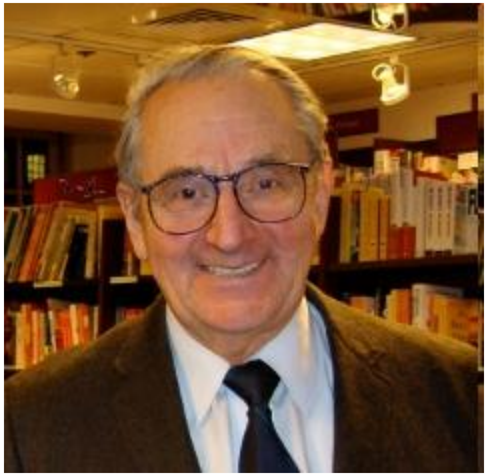
the most stable Li-organometallic is formed

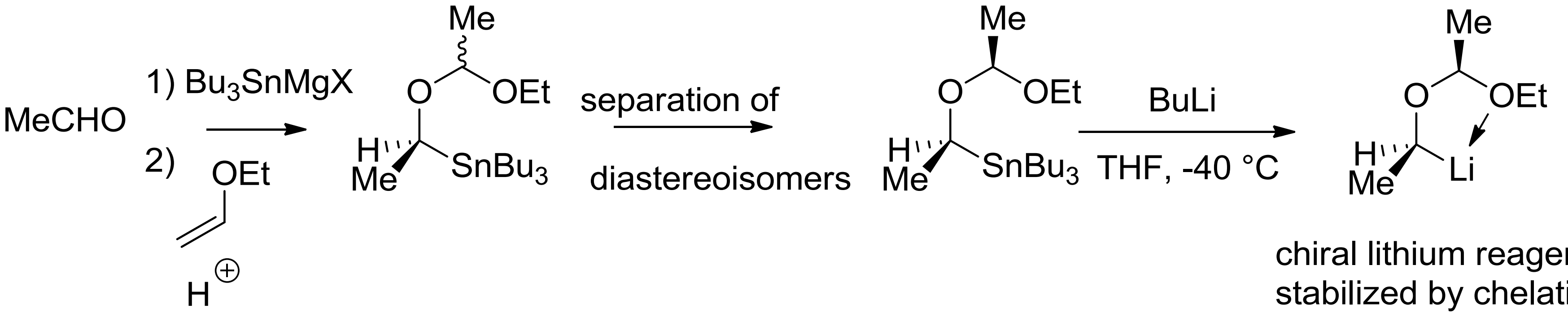


configurational stable

Li-reagent due to the ring strain

E. J. CoreyTetrahedron Lett. 1984, 25, 2415





chiral lithium reagent
stabilized by chelation

W. C. Still, *J. Am. Chem. Soc*. **1980**, *102*, 1201

Transmetalation

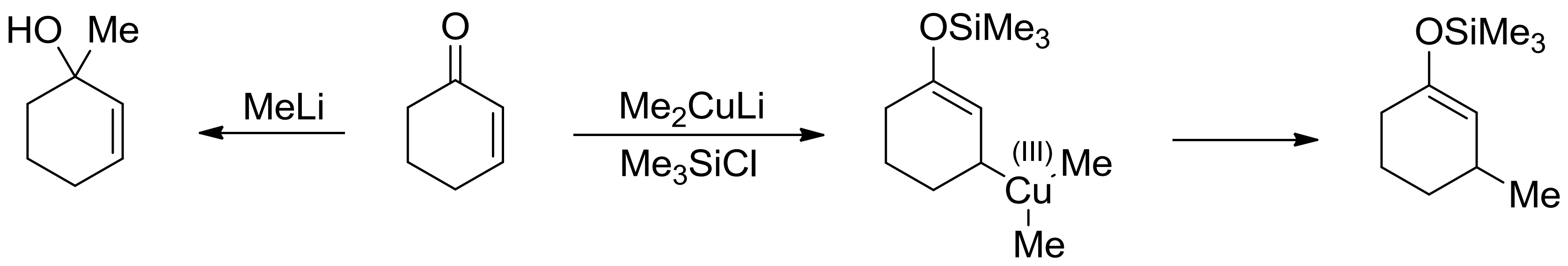
b)

$$R^1{-}Met^1 \xrightarrow{Met^2{-}X} R^1{-}Met^2$$

$$RLi + MgBr_2 \longrightarrow RMgBr + LiBr \xrightarrow{ZnCl_2} RZnX + MgX_2$$

$$Me_3TaCl_2 \xleftarrow{^3/_2\ Me_2Zn} TaCl_5 \xrightarrow[-\ 5\ LiCl]{5\ MeLi} TaMe_5$$

Transmetalation

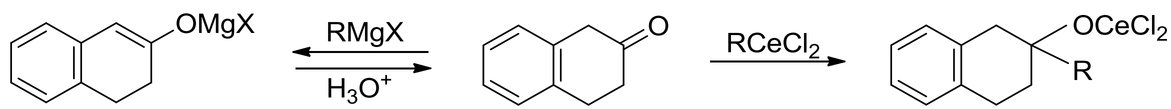


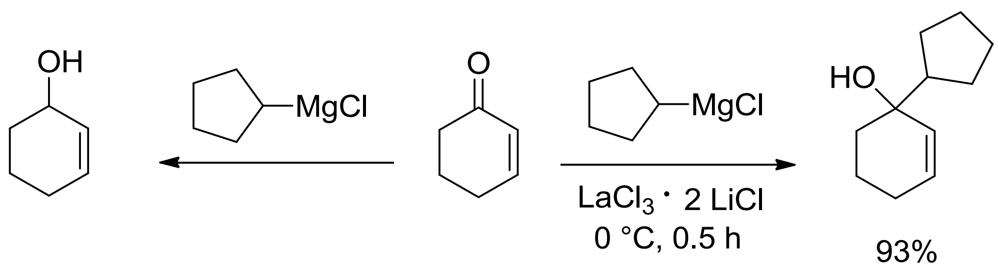
E. Nakamura, I. Kuwajima *J. Am. Chem. Soc*. **1984**, *106*, 3368

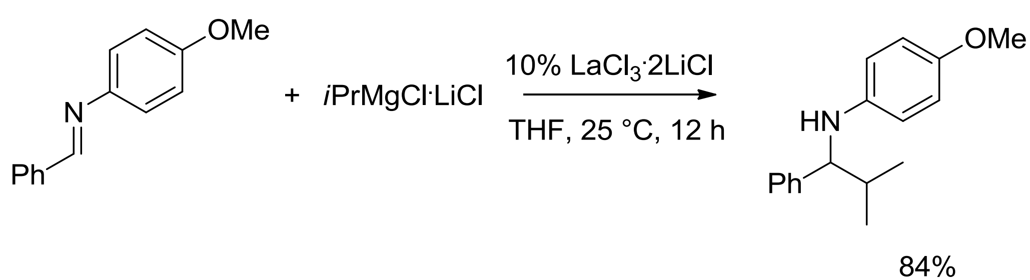
Transmetalation

$$RMgX + CeCl_3 \longrightarrow RCeCl_2 + ClMgX$$

T. Imamoto, Y. Sugiyura, N. Takiyama, *Tetrahedron Lett*. **1984**, *25*, 4233

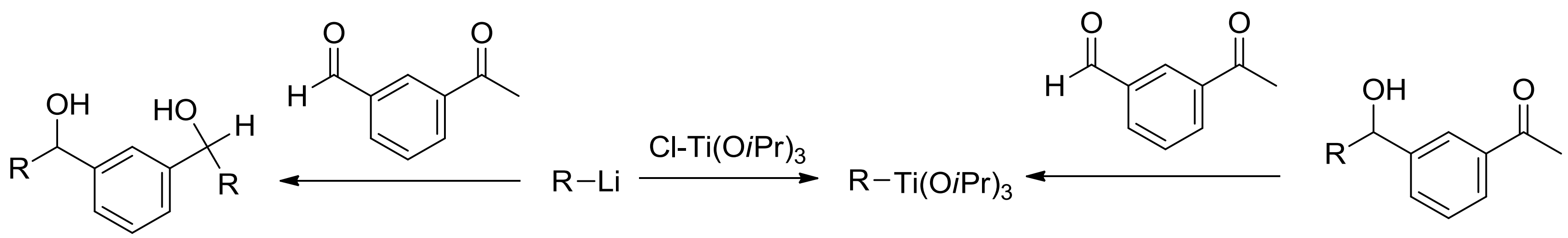






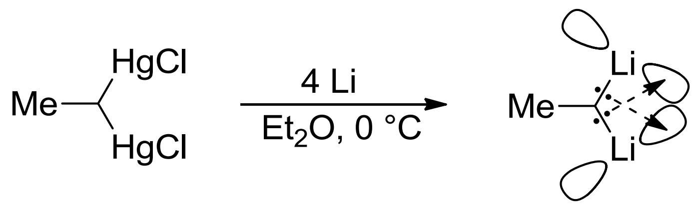
A. Krasovskiy, F. Kopp, P. Knochel *Angew. Chem. Int. Ed*. **2006**, *45*, 497

Transmetalation



M. Reetz, D. Seebach *Angew. Chem*. **1983**, *95*, 12

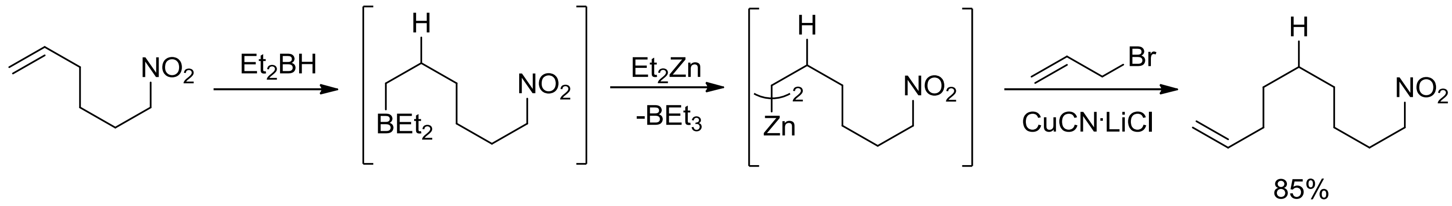
$$R^1\text{–}Met^1 \xrightarrow{Met^2} R^1\text{–}Met^2 \quad + \quad Met^1$$

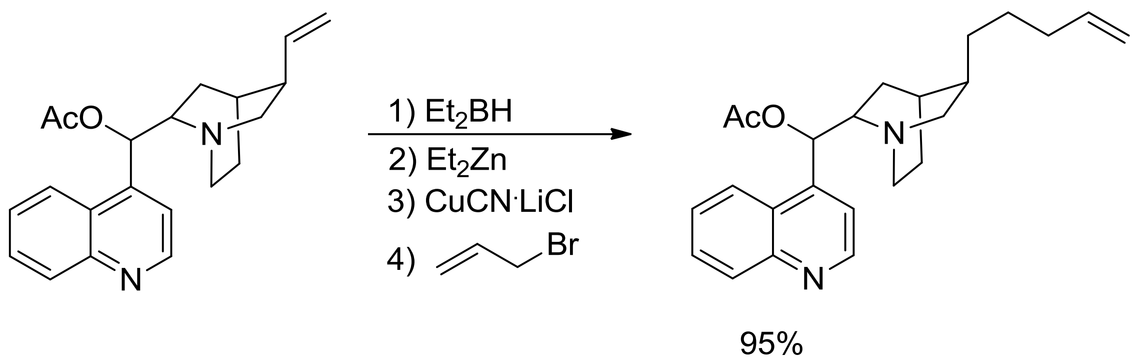


A. Maercker, M. Theis, A. Kos, P. Schleyer, *Angew. Chem*. **1983**, *95*, 755

Transmetalation

boron / zinc-exchange

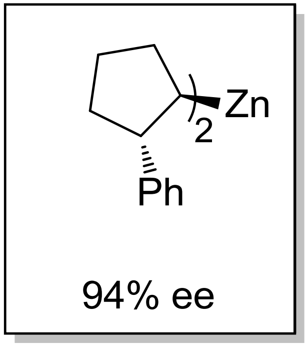


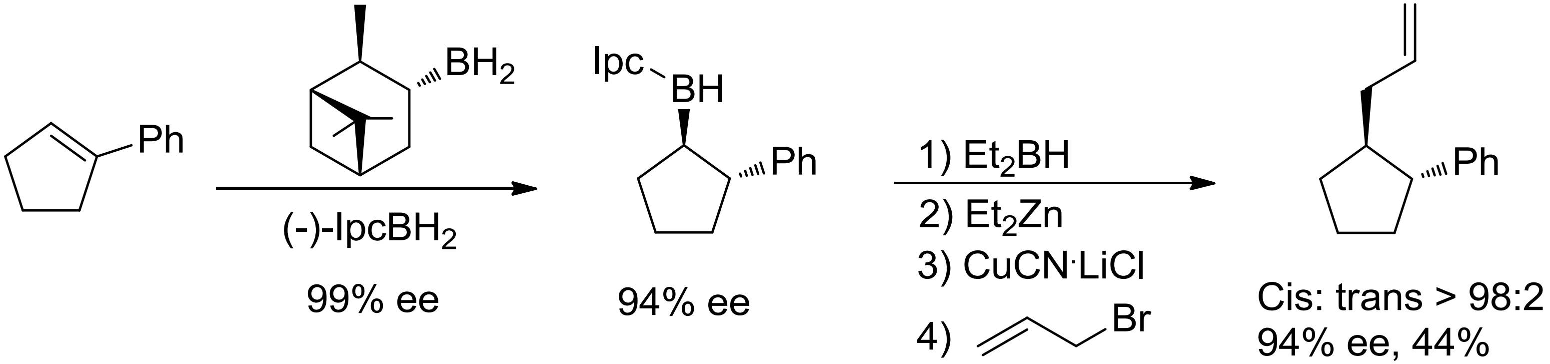


F. Langer, L. Schwink, P. Knochel *J. Org. Chem*. **1996**, *61*, 8229

Transmetalation

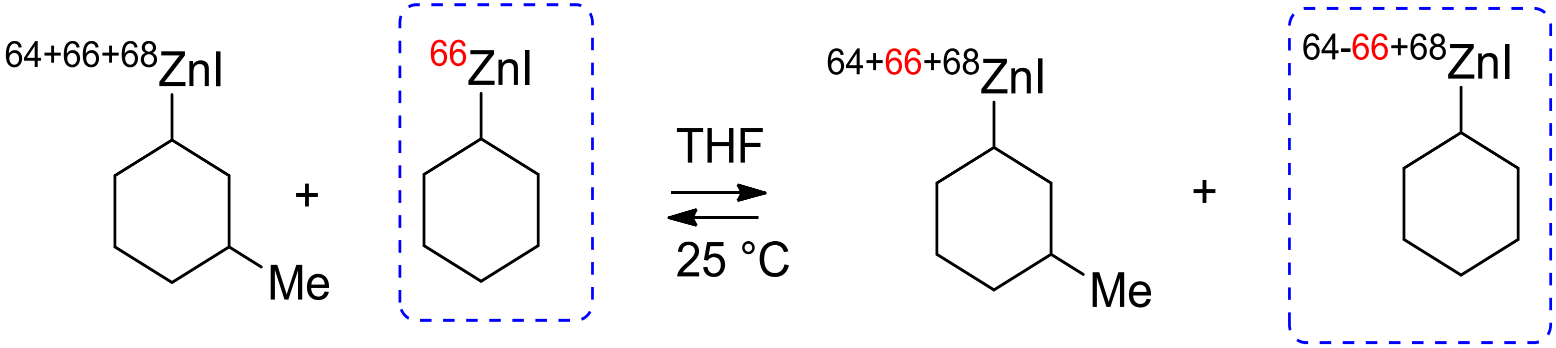
boron / zinc-exchange

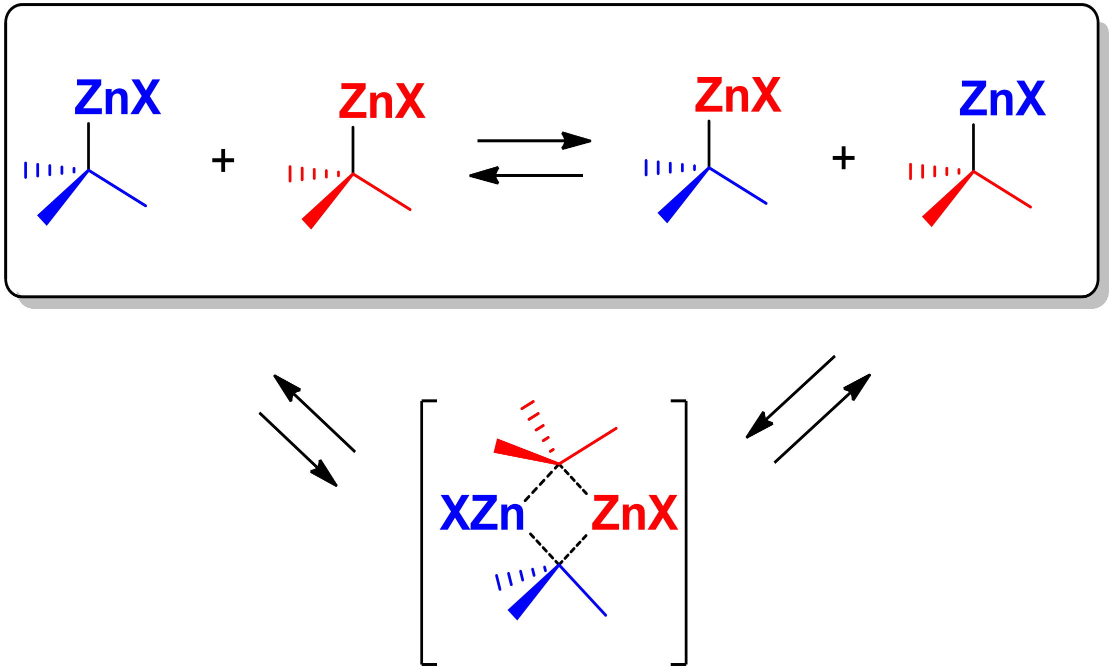




L. Micouin, M. Oestreich, P. Knochel *Angew. Chem. Int. Ed*. **1997**, *36*, 245

Nature of the carbon-zinc bond





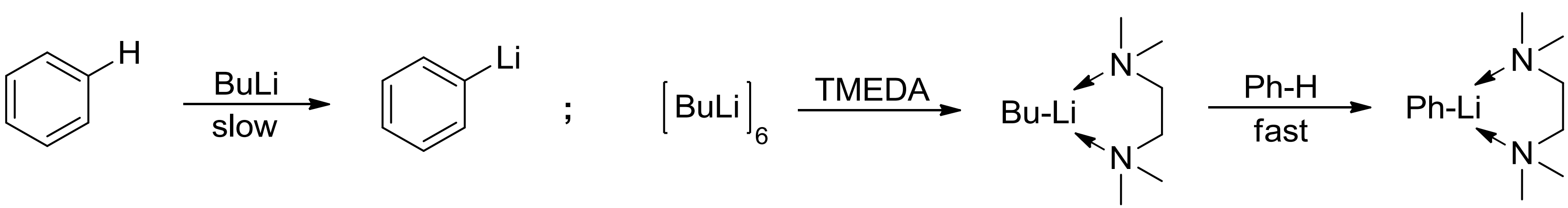
Metalation (starting from a compound with an acid proton)

$$R^2\text{-H} \xrightarrow{R^1\text{-Met}} R^2\text{-Met}$$

$R^{2\ominus}$ must be more stable than $R^{1\ominus}$ $\Longrightarrow$ pKa(R^1-H) > pKa(R^2-H) (thermodynamic criteria)

R^1–Met : *t*-BuOK, LDA, BuLi, ...

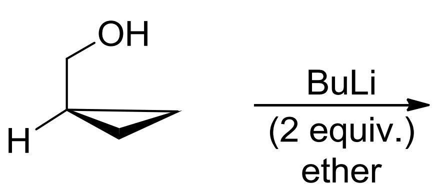
kinetic criteria (kinetic acidity)

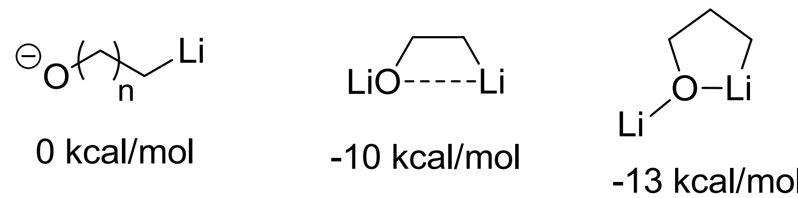


$PhCH_2Li$ reacts with benzene 10^4 times faster than with MeLi

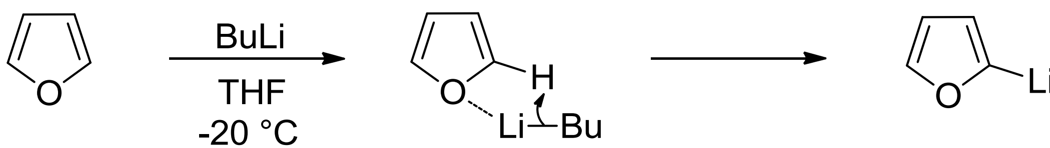
$PhCH_2Li$ is a monomer in THF, MeLi a tetramer

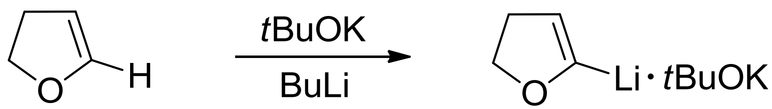
Directed metalation

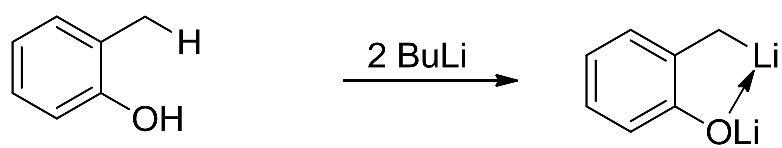




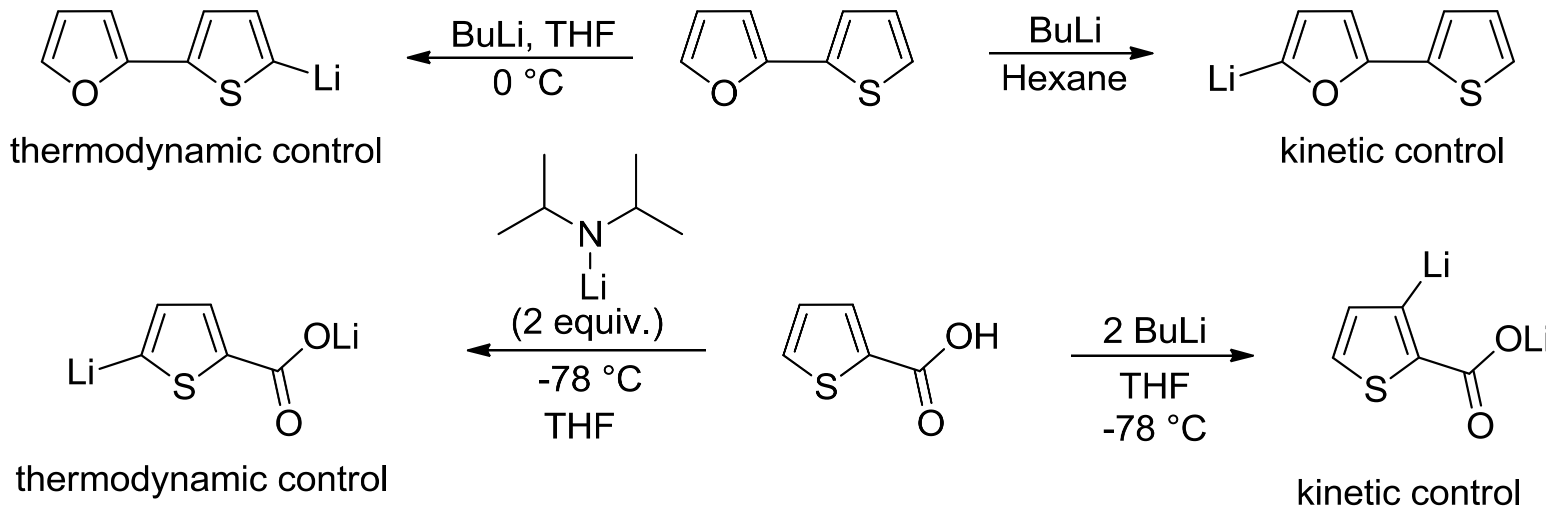
Directed metalation



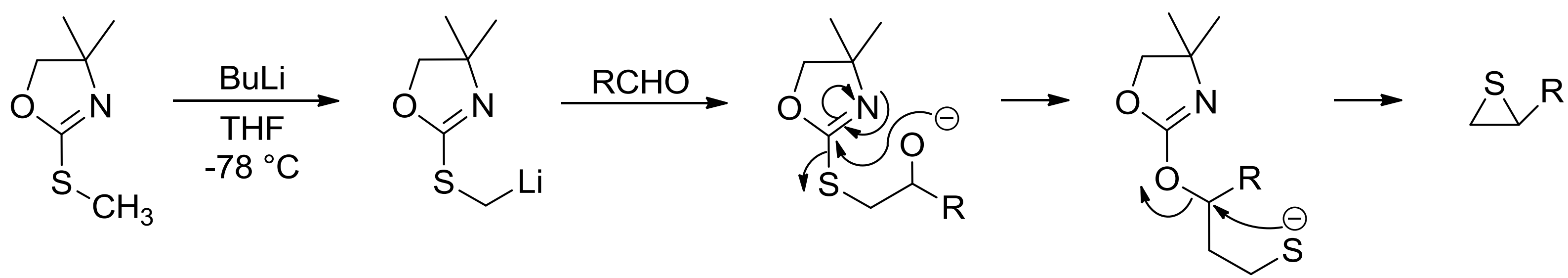




Metalation

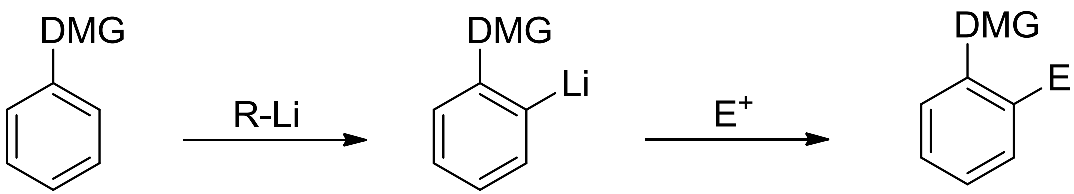


rearrangement



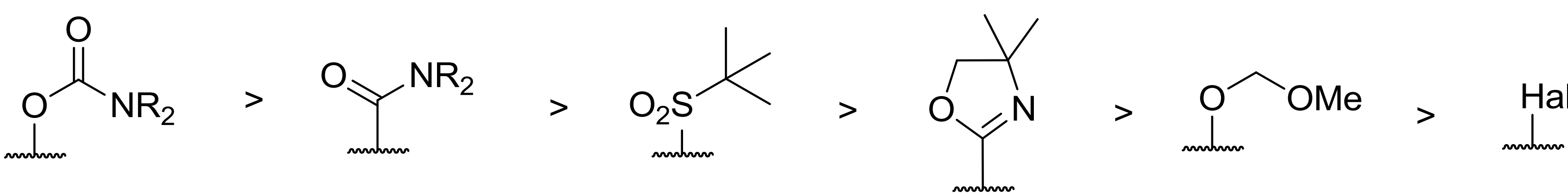
Metalation

directed lithiation



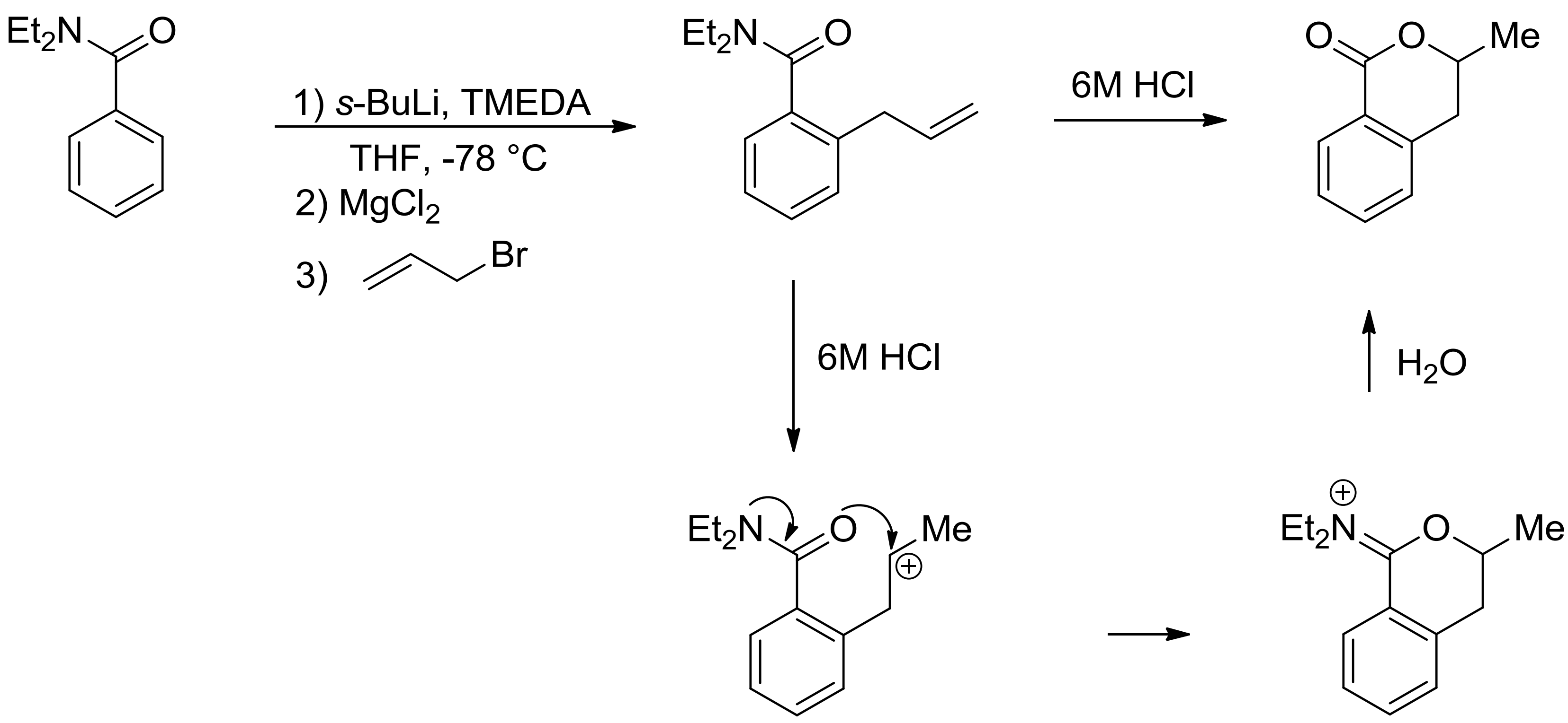
DMG = directing metalating group

V. Snieckus, *Chem Rev*. **1990**, *90*, 879

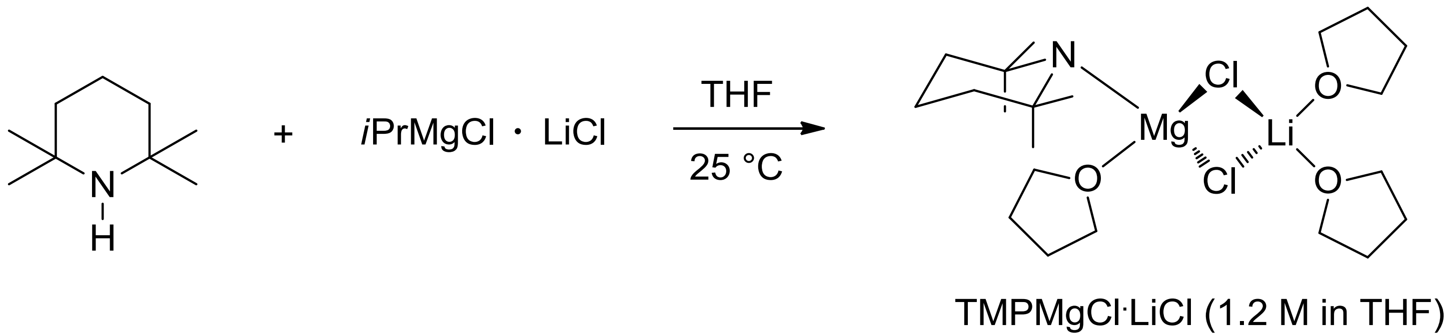


P. Beak, V. Snieckus, *Angew. Chem. Int. Ed*. **2004**, *43*, 2206

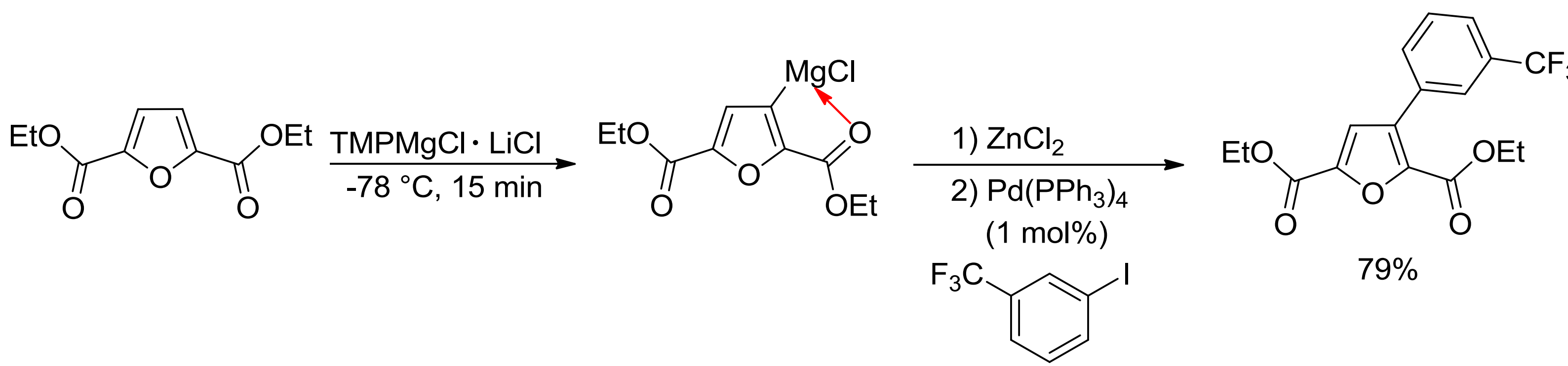
Metalation


Et2N
O
1) s-BuLi, TMEDA
THF, -78 °C
2) MgCl2
3)
Br
Et2N
O
6M HCl
O
O
Me
6M HCl
H2O
Et2N
O
Me
Et2N
O
Me

Metalation

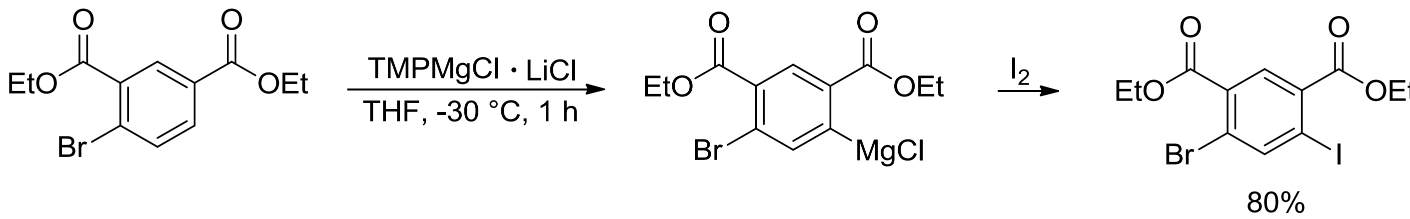


A. Krasovskiy, P. Knochel *Angew. Chem. Int. Ed*. **2006**, *45*, 2958
R. E. Mulvey, *Angew. Chem. Int. Ed*. **2008**, *47*, 8079

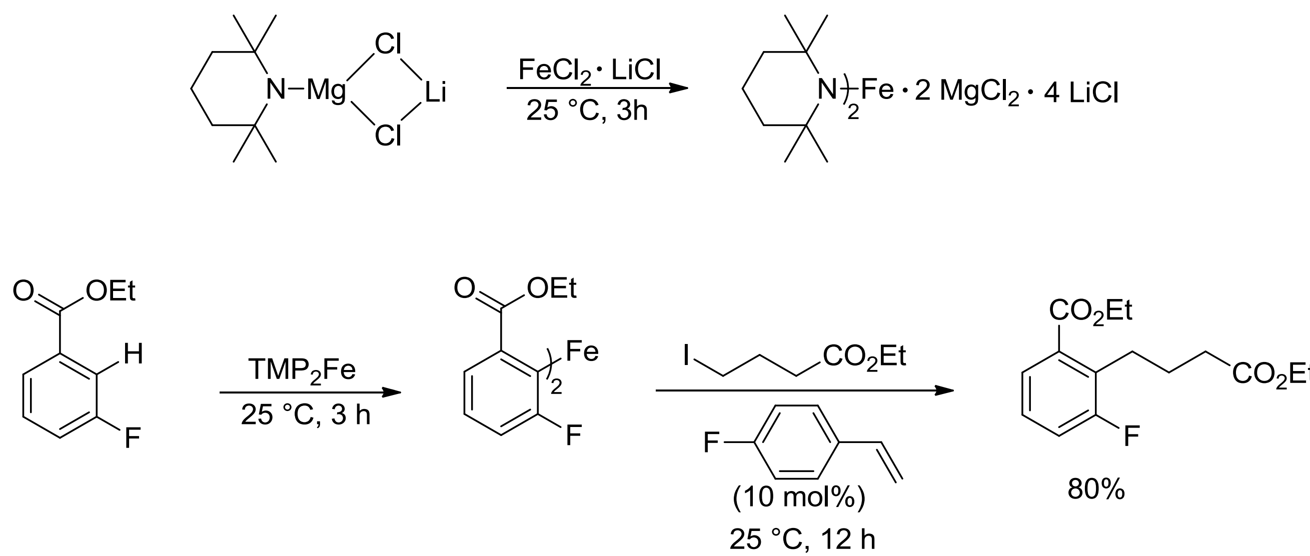


F. M. Piller, P. Knochel *Org. Lett*. **2009**, *11*, 445

Metalation

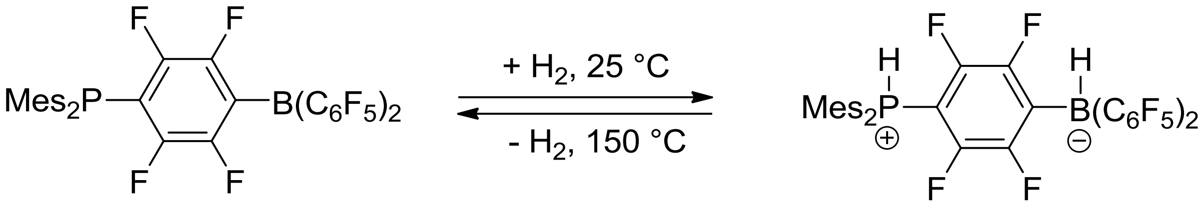


O. Baron, P. Knochel *Angew. Chem. Int. Ed*. **2006**, *45*, 2958

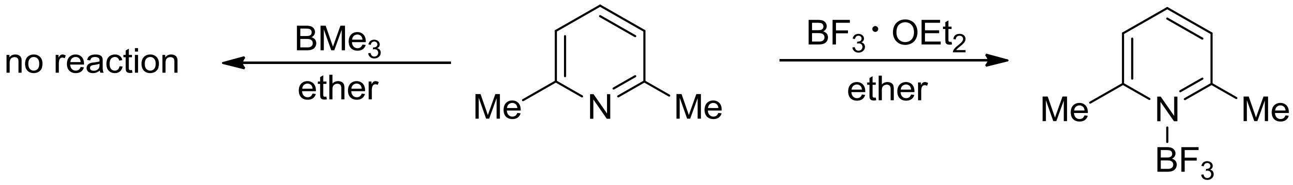


S. Wunderlich, P. Knochel *Angew. Chem. Int. Ed*. **2009**, *48*, 9717

Frustrated Lewis Pairs

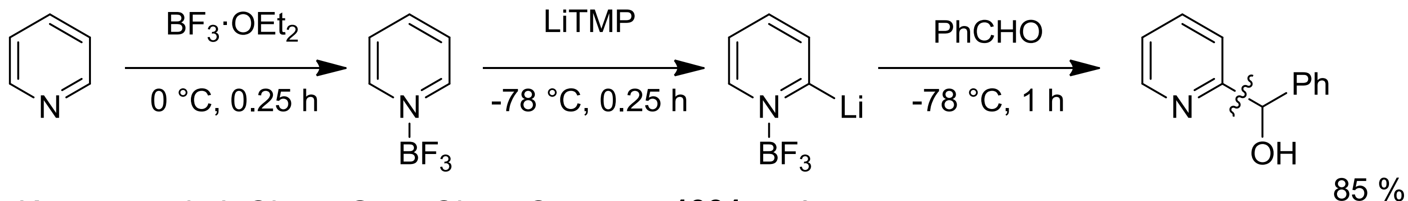


D. Stefan, G. Erker *Angew. Chem. Int. Ed*. **2010**, *49*, 46

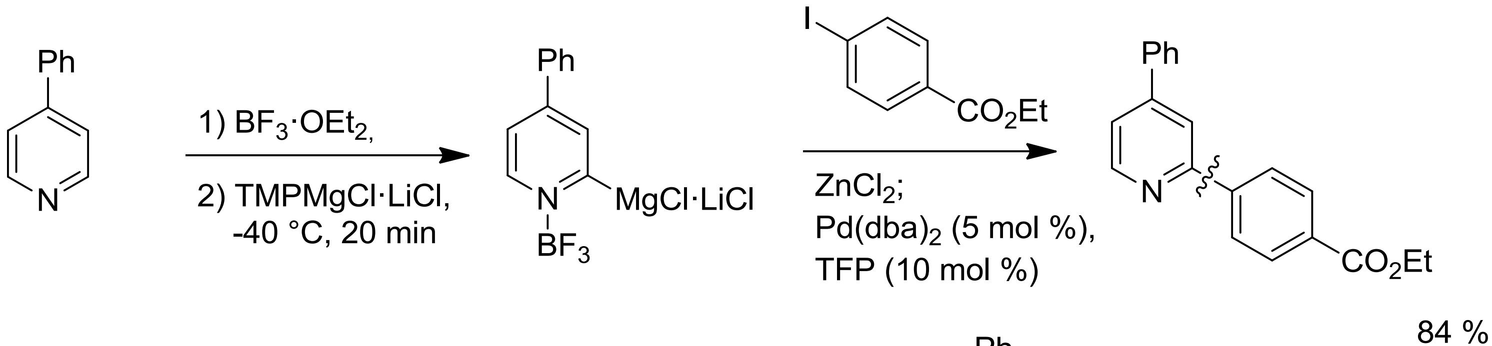


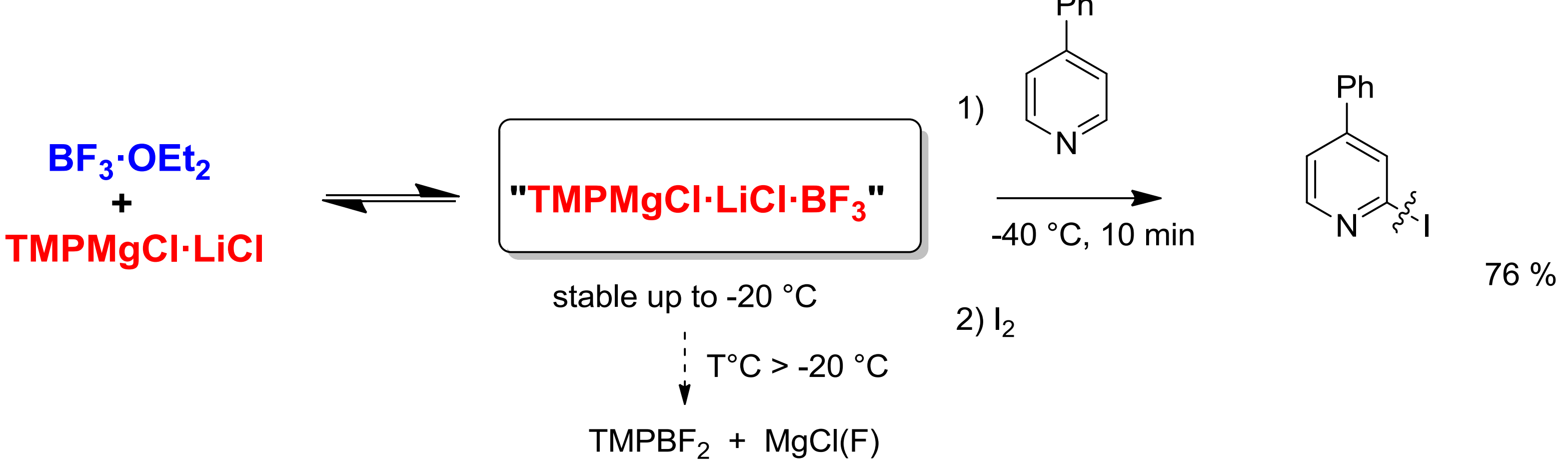
H. C. Brown *J. Am. Chem. Soc*. **1942**, *64*, 325

Frustrated Lewis Pairs



Kessar *et al, J. Chem. Soc., Chem Commun.* **1991**, 570

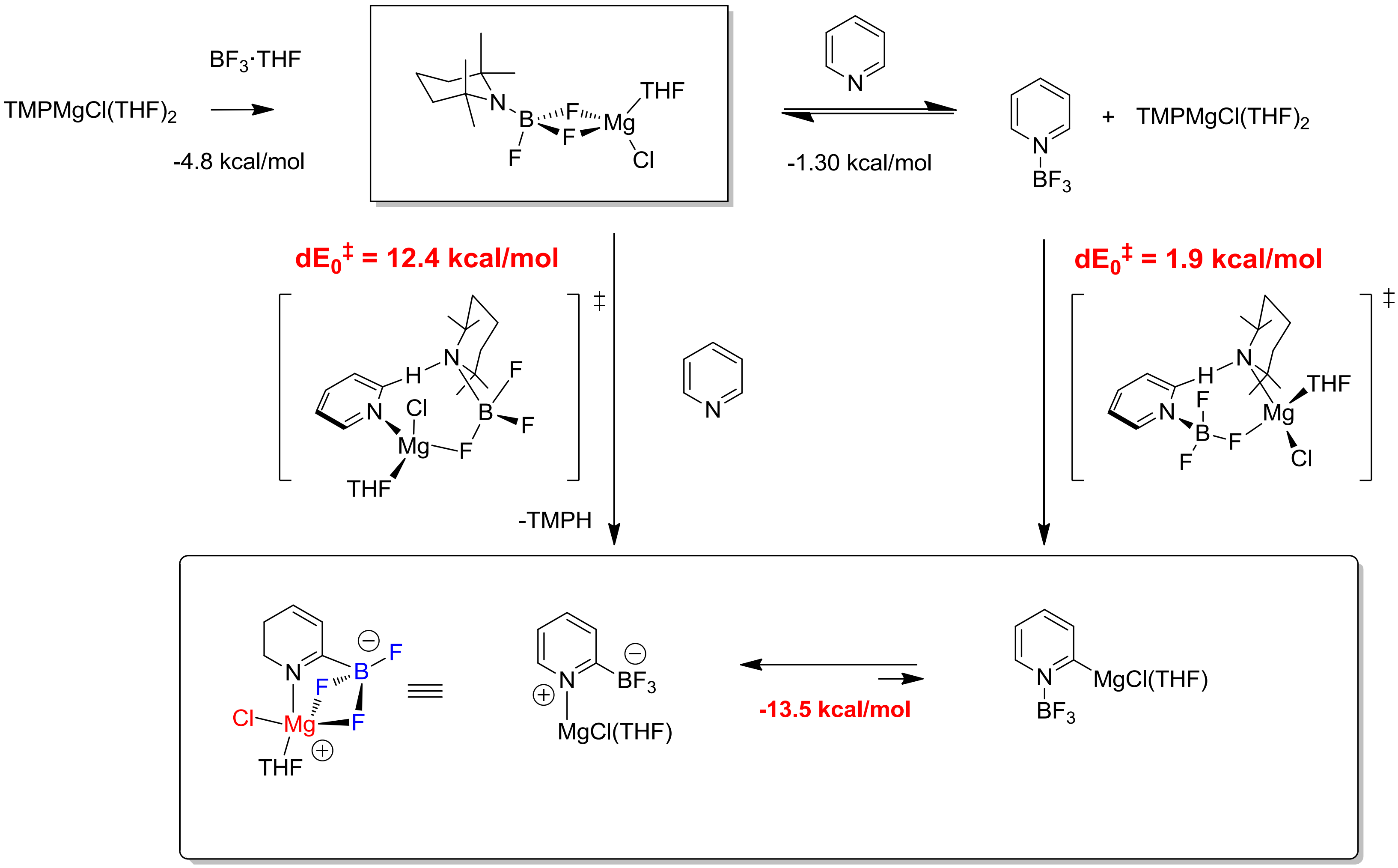




M. Jaric, B. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel *Angew. Chem. Int. Ed.* **2010**, *49*, 5451

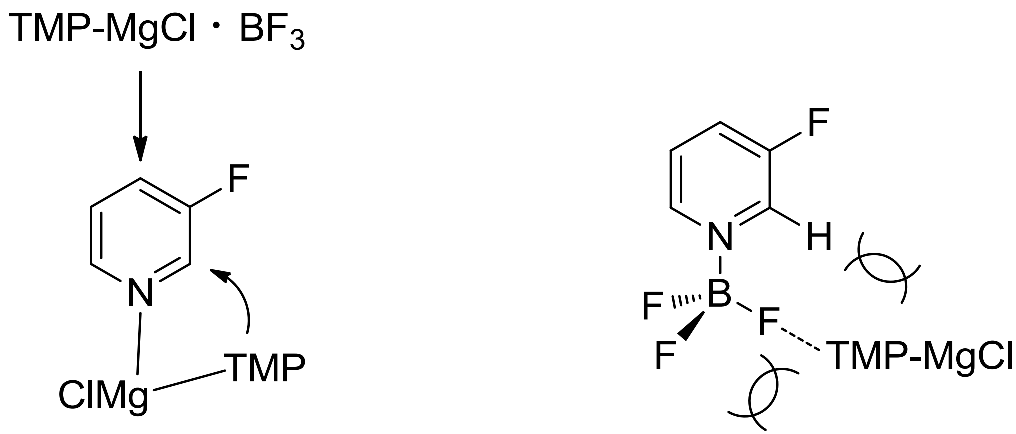
Frustrated Lewis Pairs

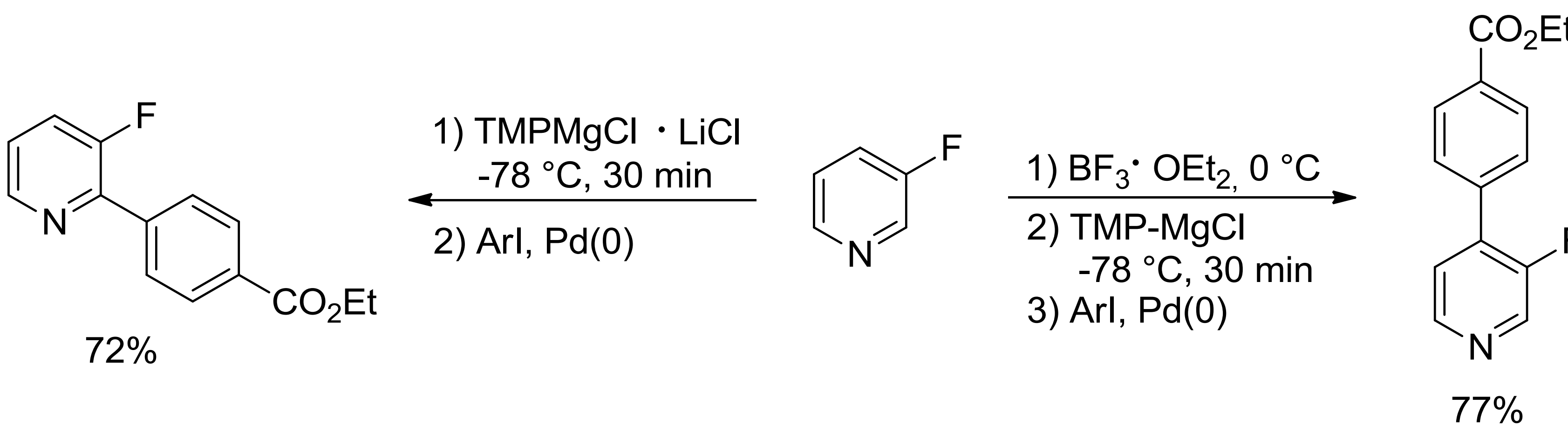
B3LYP/6-31G,def2-SVP**



M. Jaric, B. Haag, A. Unsinn, K. Karaghiosoff, P. Knochel *Angew. Chem. Int. Ed.* **2010**, *49*, 5451

Frustrated Lewis Pairs



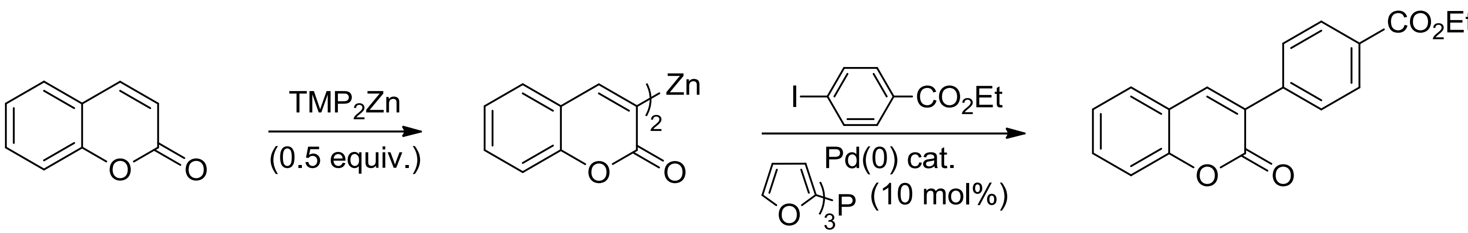


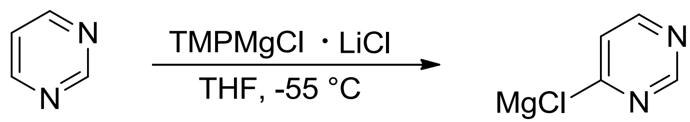
Jaric, M.; Haag, B. A.; Unsinn, A.; Karaghiosoff, K.; Knochel, P *Angew. Chem. Int. Ed.* **2010**, *49*, 5451.

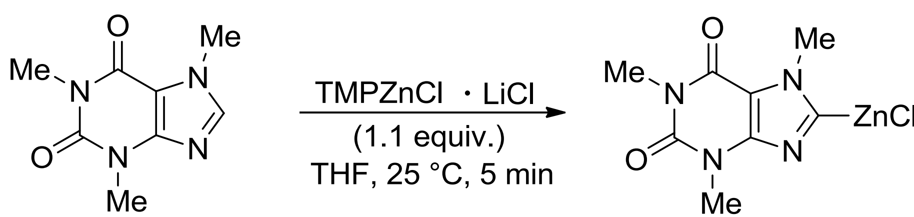
Metalation

$$\text{TMP-MgCl} \cdot \text{LiCl} \xrightarrow[\text{THF, 25 °C, 15 h}]{\text{ZnCl}_2} \text{TMP}_2\text{Zn} \cdot 2\text{LiCl} \cdot 2\text{MgCl}_2$$

S. Wunderlich, P. Knochel *Angew. Chem. Int. Ed*. **2007**, *46*, 7685

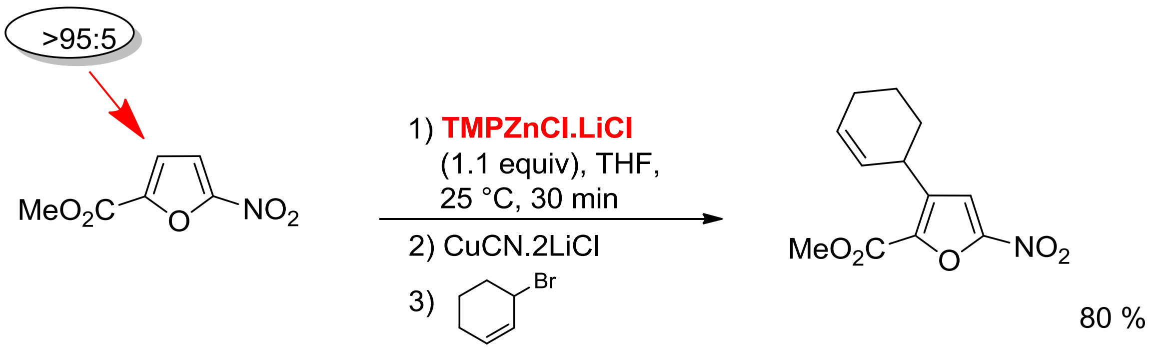


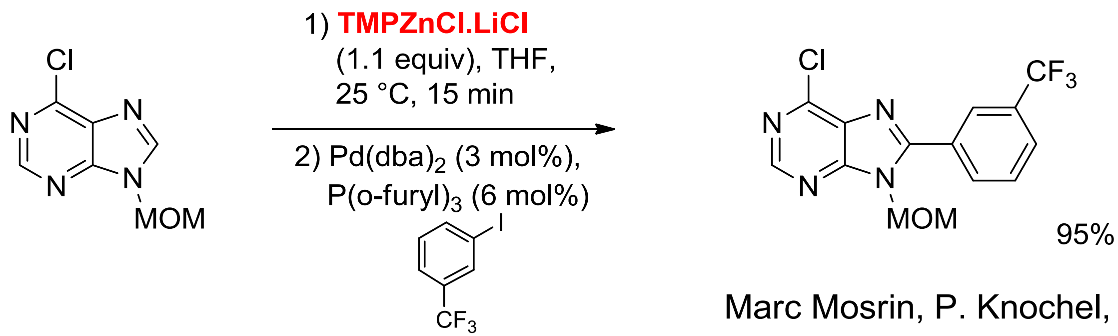




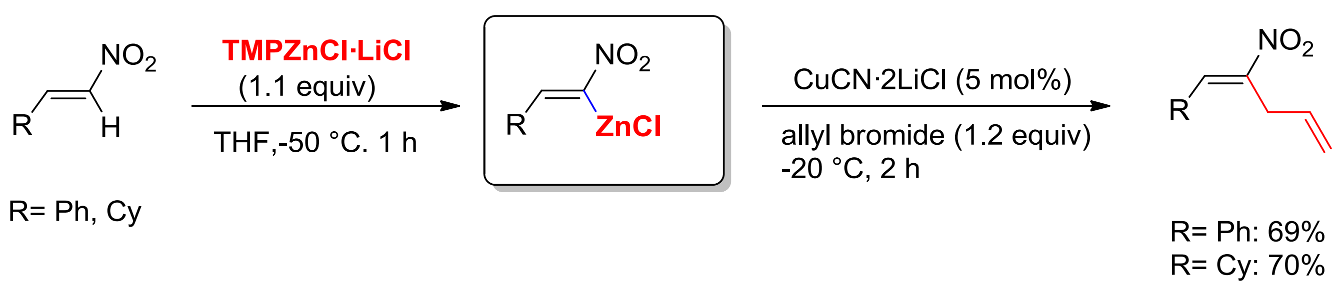
M. Mosrin, P. Knochel *Org. Lett*. **2008**, *10*, 2497
M. Mosrin, P. Knochel *Chem. Eur. J*. **2009**, *15*, 1468
M. Mosrin, P. Knochel *Org. Lett*. **2009**, *11*, 1837

Zincations in the presence of ester and nitro groups



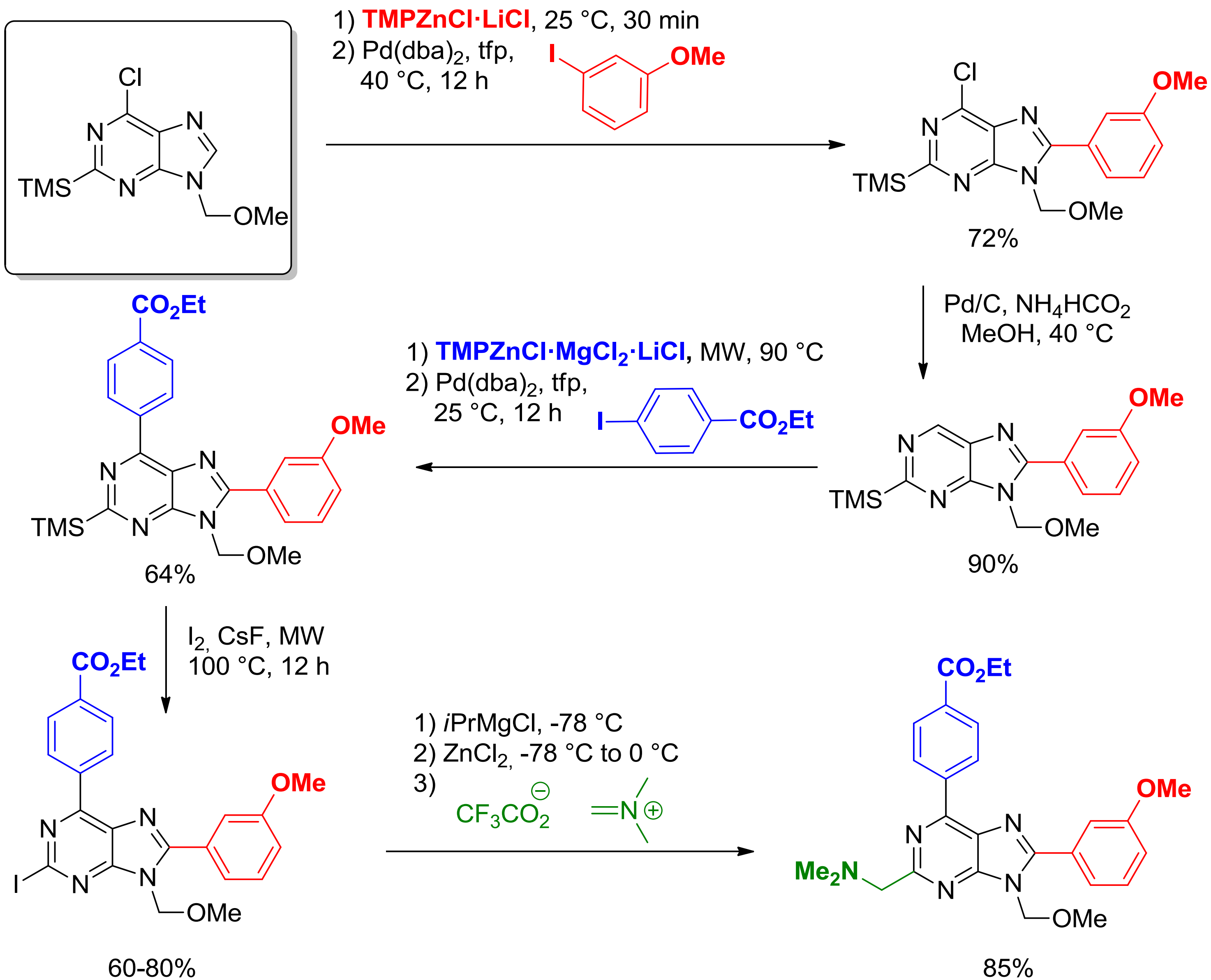


Marc Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837-1840.



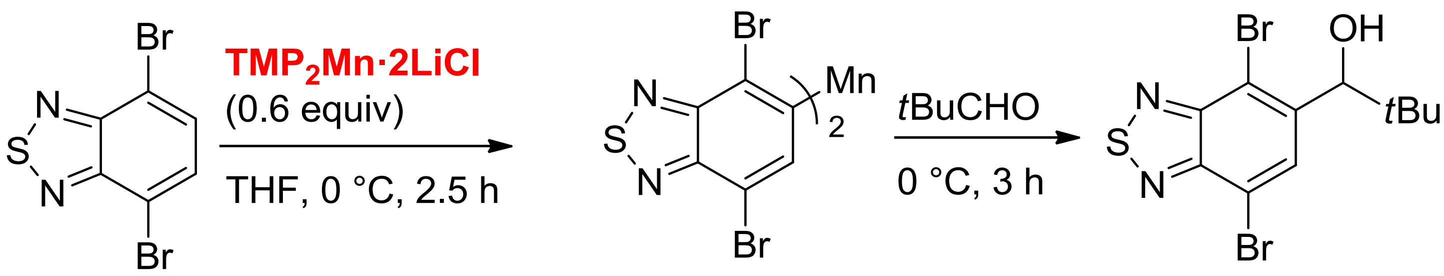
Tomke Bresser, P. Knochel, *Angew. Chem. Int. Ed.* **2011**, *50,* 1914

Trifunctionalization of the purine scaffold using Mg and Zn organometallics

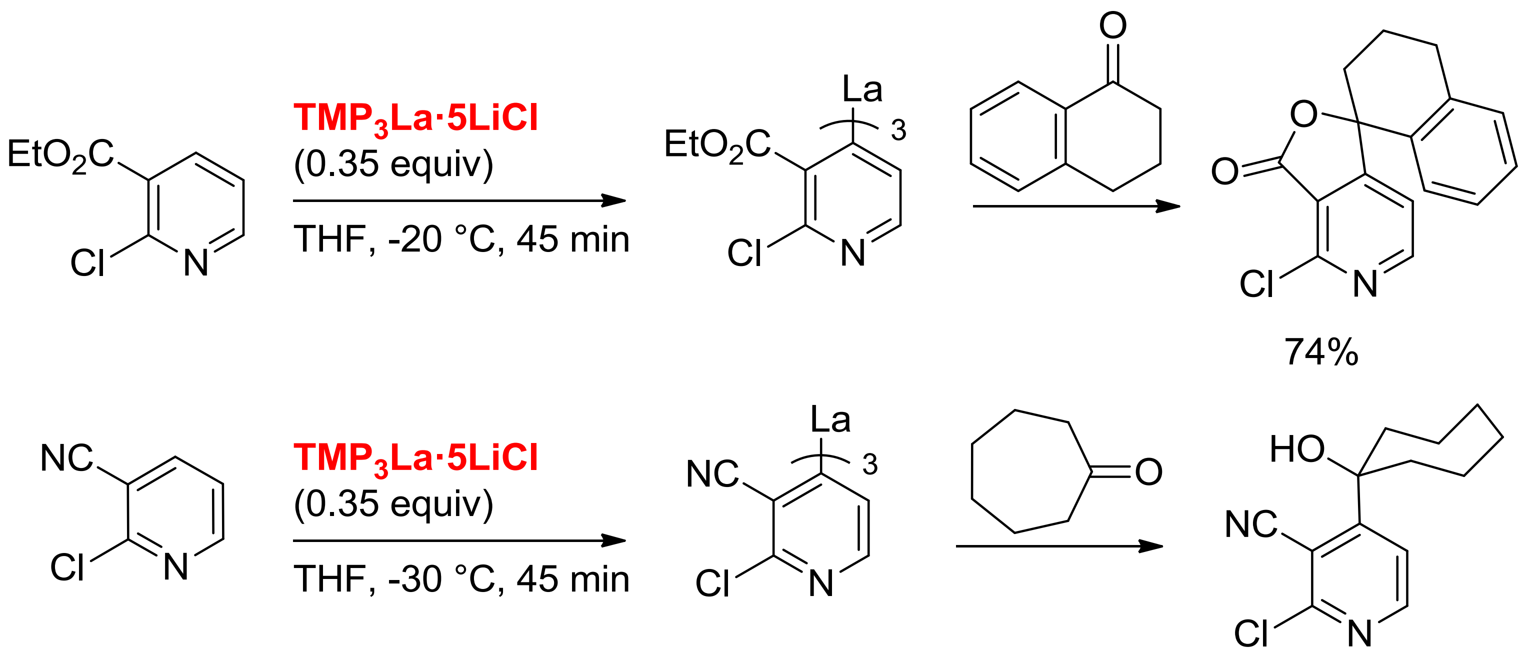


S. Zimdars; X. Mollat du Jourdin; F. Crestey; T. Carell; P. Knochel. *Org. Lett*, **2011**, *13*, 792–795

Lanthanations and manganation of heterocycles

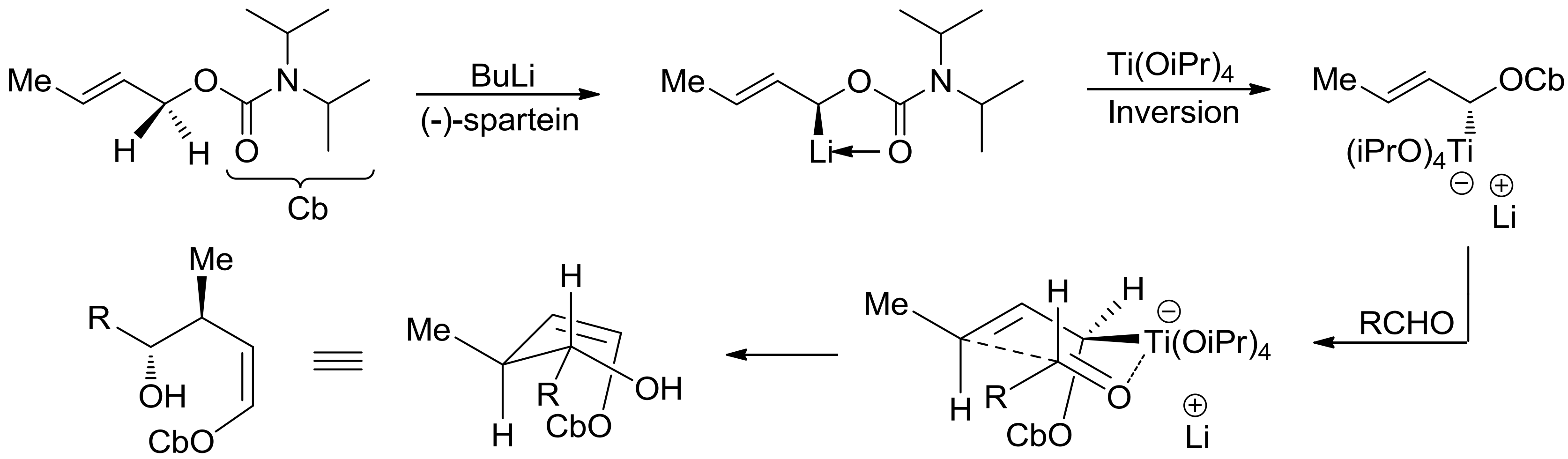


S. Wunderlich, M. Kienle, P. Knochel, *Angew. Chem. Int. Ed.* **2009**, *48*, 7256.



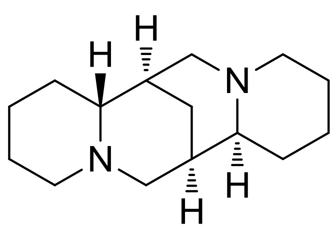
S. H. Wunderlich, P. Knochel, *Chem. Eur. J.* **2010**, *16*, 3304-3307.

Asymmetric metalation using (*S*)-(-)-spartein

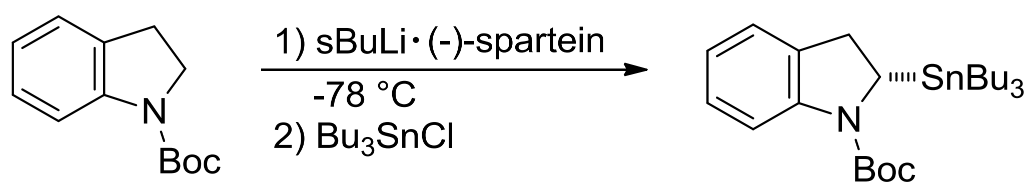


82-92% ee

D. Hoppe, et al. *Pure Appl. Chem*. **1994**, *66*, 1479.



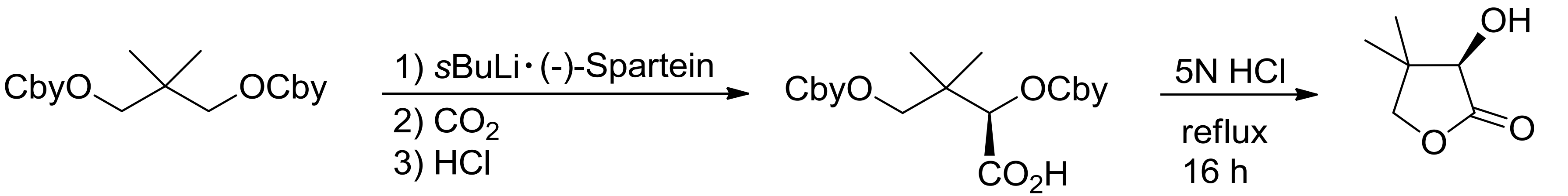
(S)-(-)-spartein



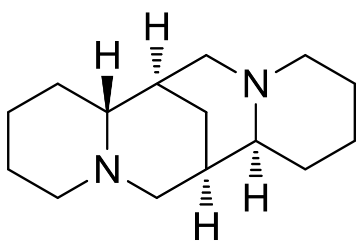
98% ee

P. Beak *J. Org. Chem*. **1997**, *62*, 7679

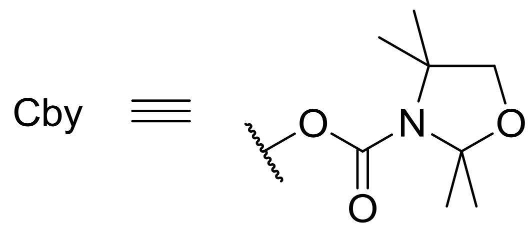
Asymmetric metalation using (*S*)-(-)-spartein



73%; > 95 %ee

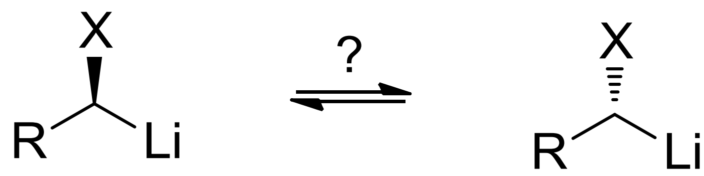


(S)-(-)-Spartein

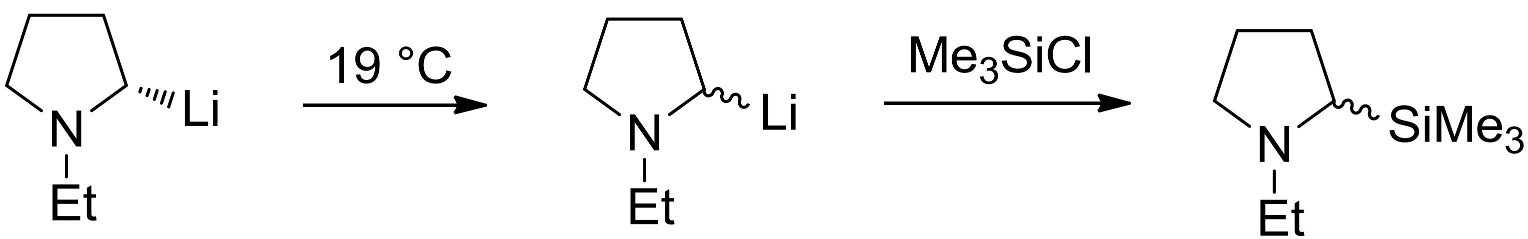


D. Hoppe *Tetrahedron Lett*. **1992**, *33*, 5327

Configurational stability

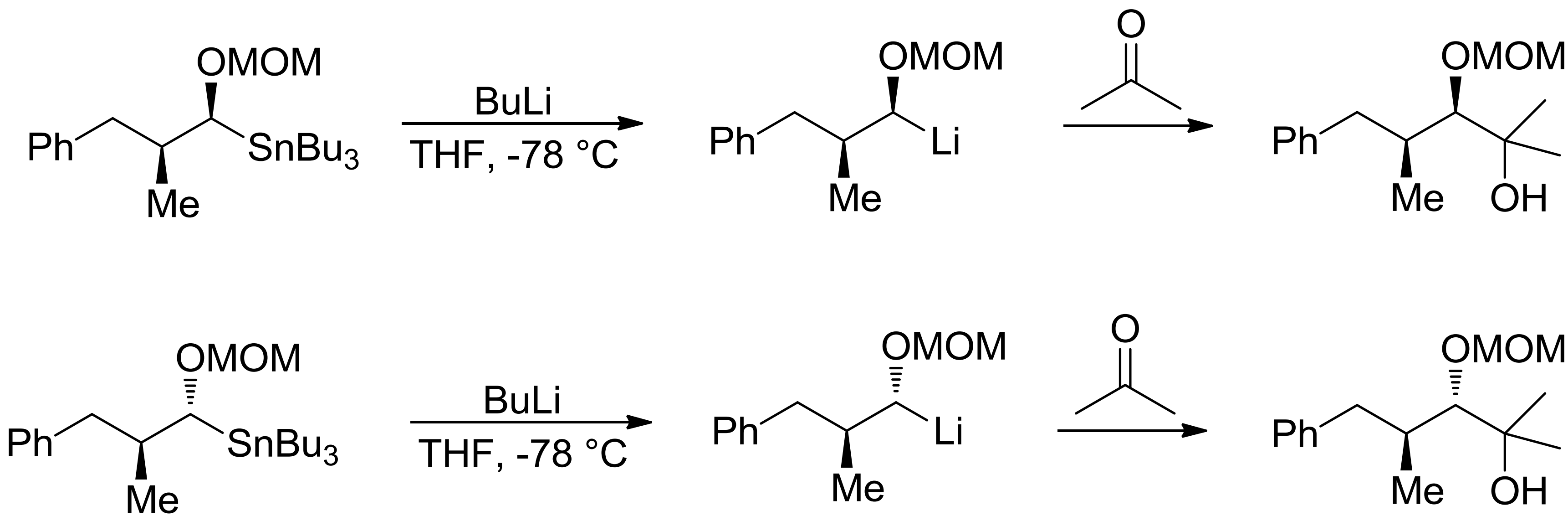


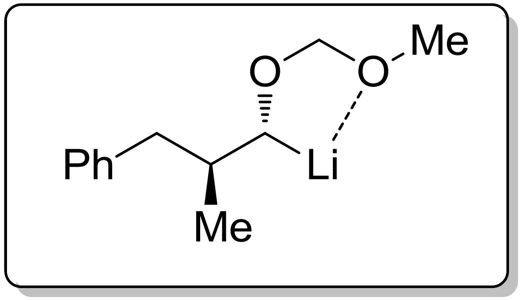
X=Br, SePh, SPh, OCH_2OMe, $OCONiPr_2$



R. E. Gawley, *J. Am. Chem. Soc*. **2005**, *127*, 449

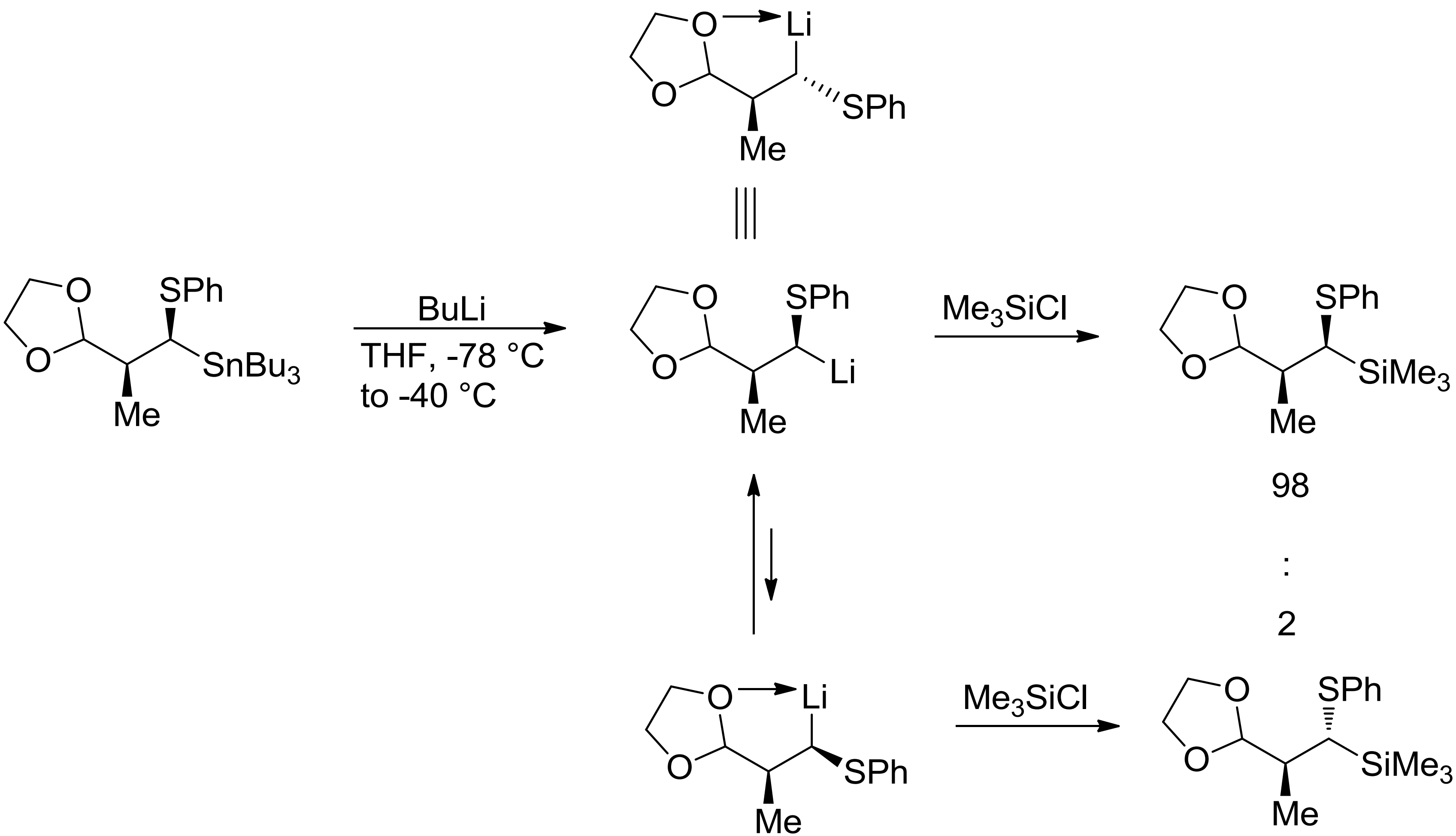
Diastereoselective transmetalation





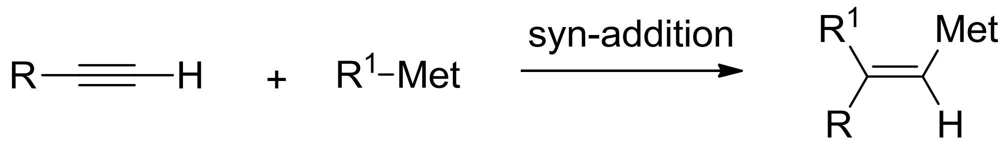
W. C. Still J. *Am. Chem. Soc*. **1980**, *102*, 1201

Diastereoselective transmetalation

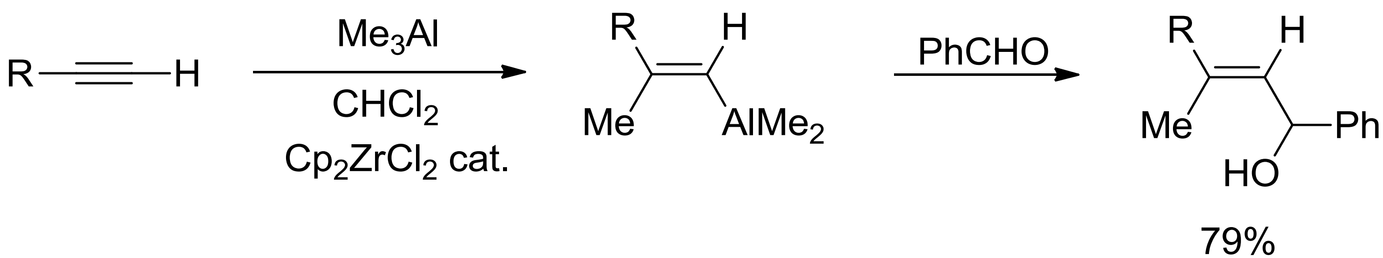


P. G. McDougal, *Tetrahedron Lett*. **1988**, *29*, 2547

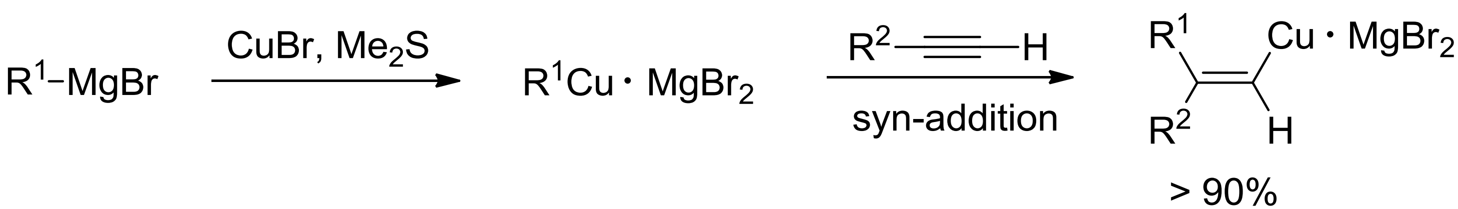
Carbometalation



Negishi-reaction: carboalumination



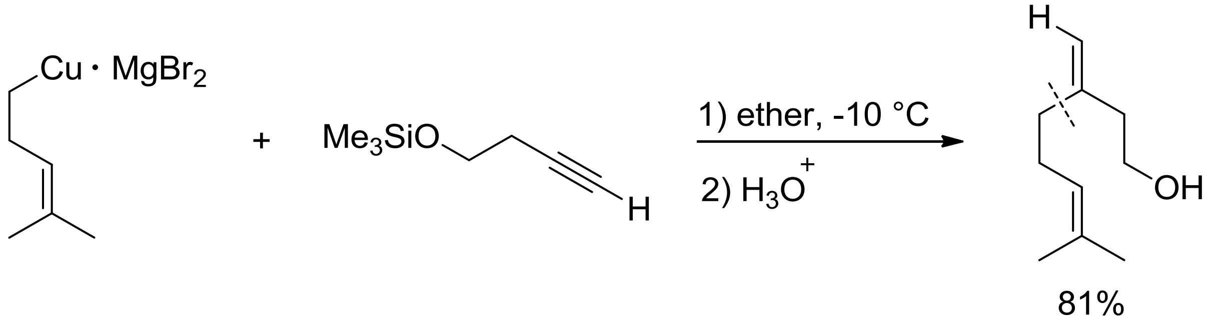
E. Negishi *J. Am. Chem. Soc*. **1976**, *98*, 6729



Normant-reaction: carbocupration

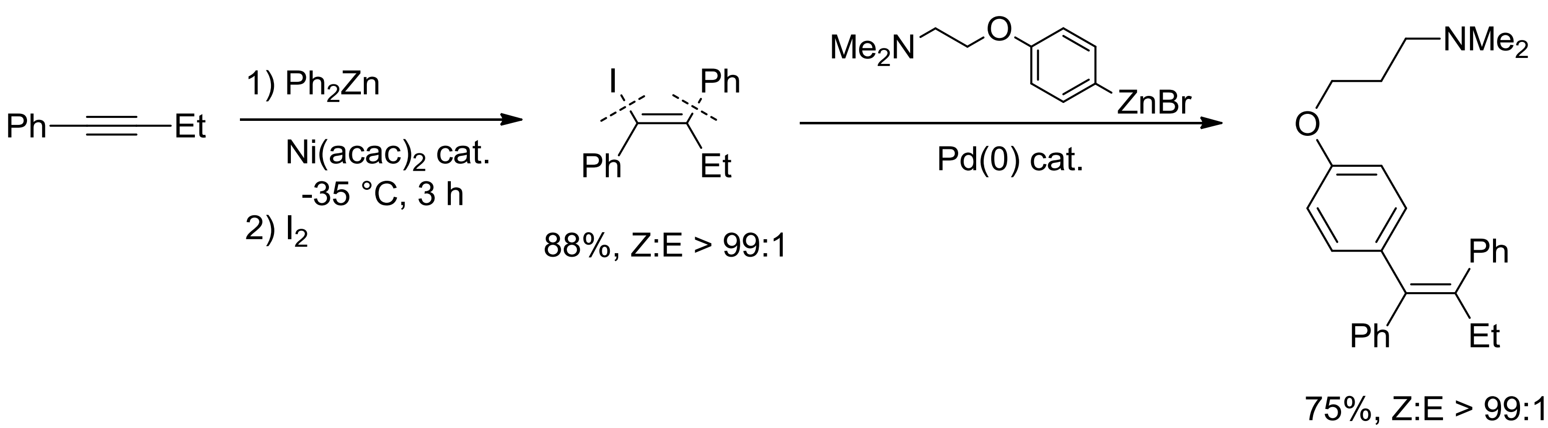
Review: A. Alexakis, J. F. Normant, *Synthesis* **1981**, 841.

Carbometalation



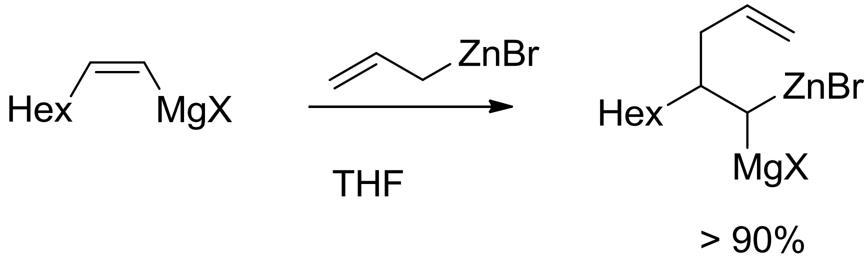
A. Alexakis, J. F. Normant, *J. Organomet. Chem*. **1975**, *96*, 471

Tamoxifen-Synthesis: Carbozincation

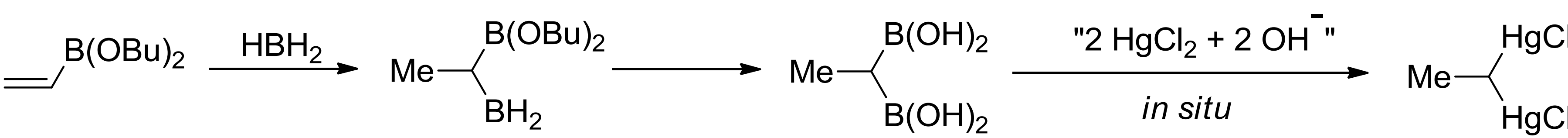


T. Stüdemann, P. Knochel *Angew. Chem*. **1997**, *109*, 132

Carbometalation, hydrometalation



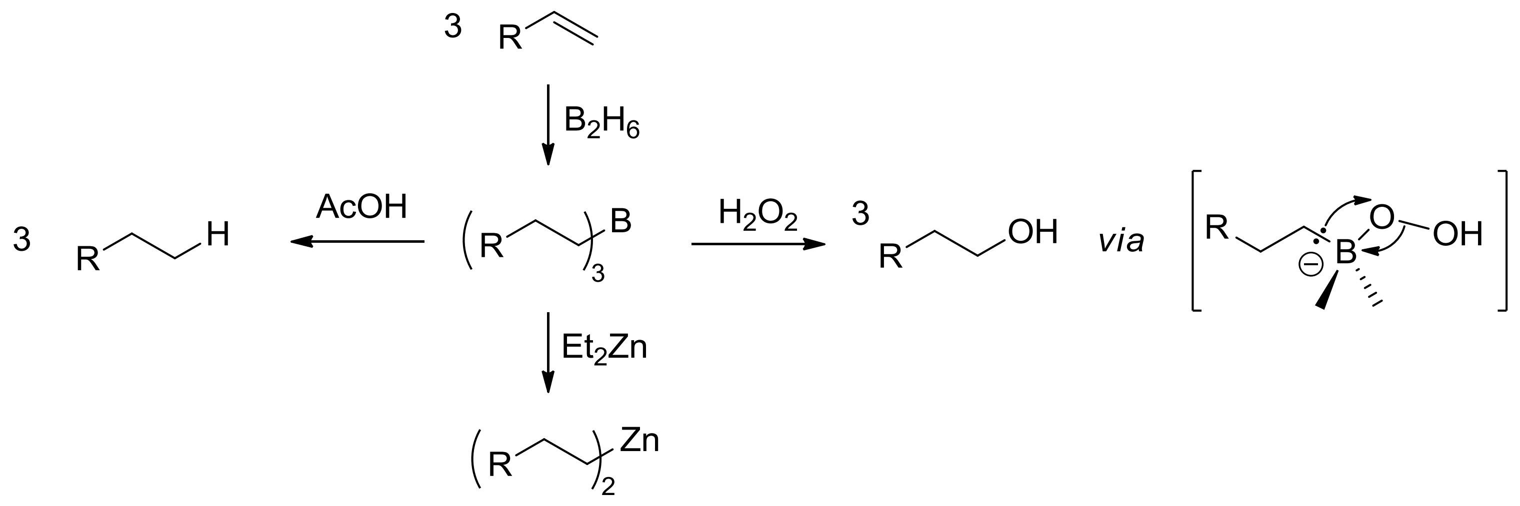
P. Knochel, J. F. Normant *Tetrahedron Lett*. **1986**, *27*, 1039; 1043; 4427

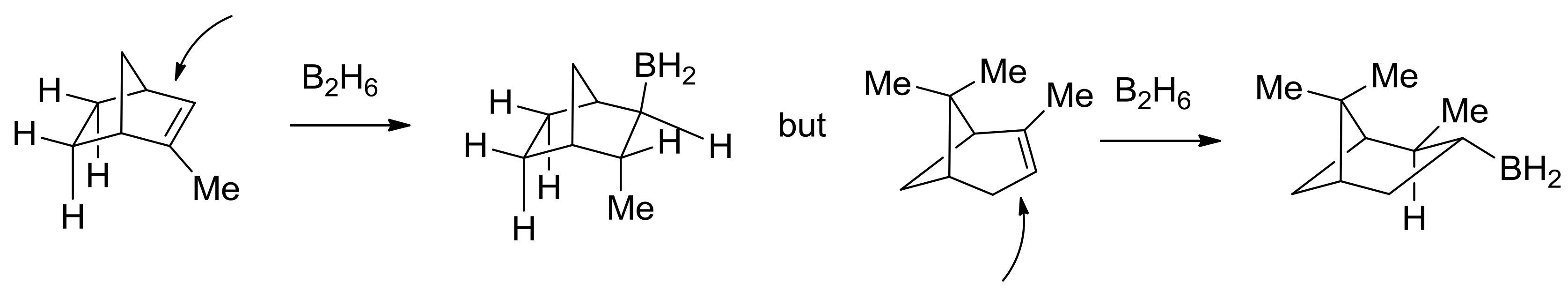


D. Matteson, *J. Org. Chem*. **1964**, *29*, 2742

Hydrometalation and application of organoboranes in organic chemistry

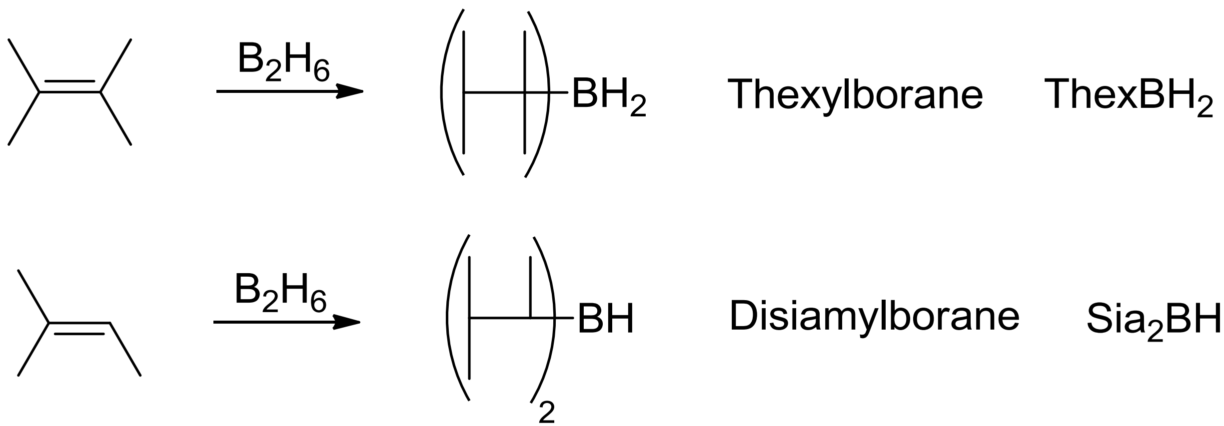
hydroboration





Hydroboration

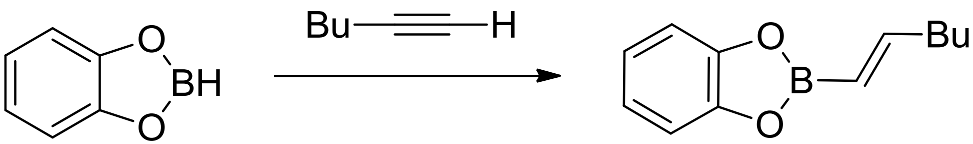
selective hydroborating reagents



H. C. Brown, E. Negishi *J. Am. Chem. Soc*. **1975**, *97*, 2799

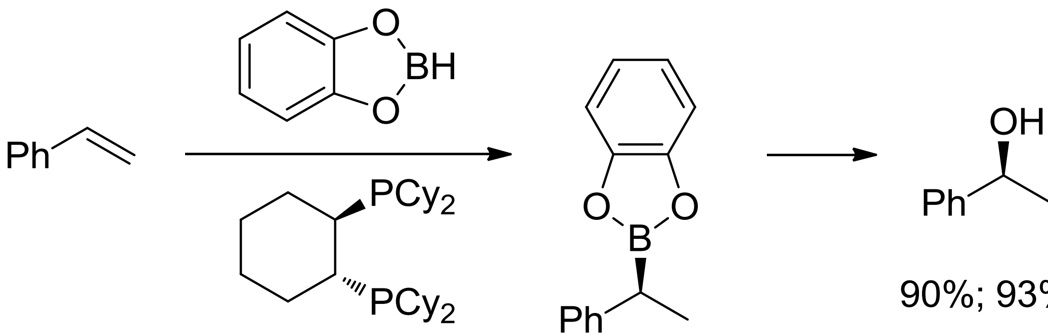
Hydroboration

catecholborane



>90%

A. Arase, et al., *Synth. Comm*. **1995**, *25*, 1957.



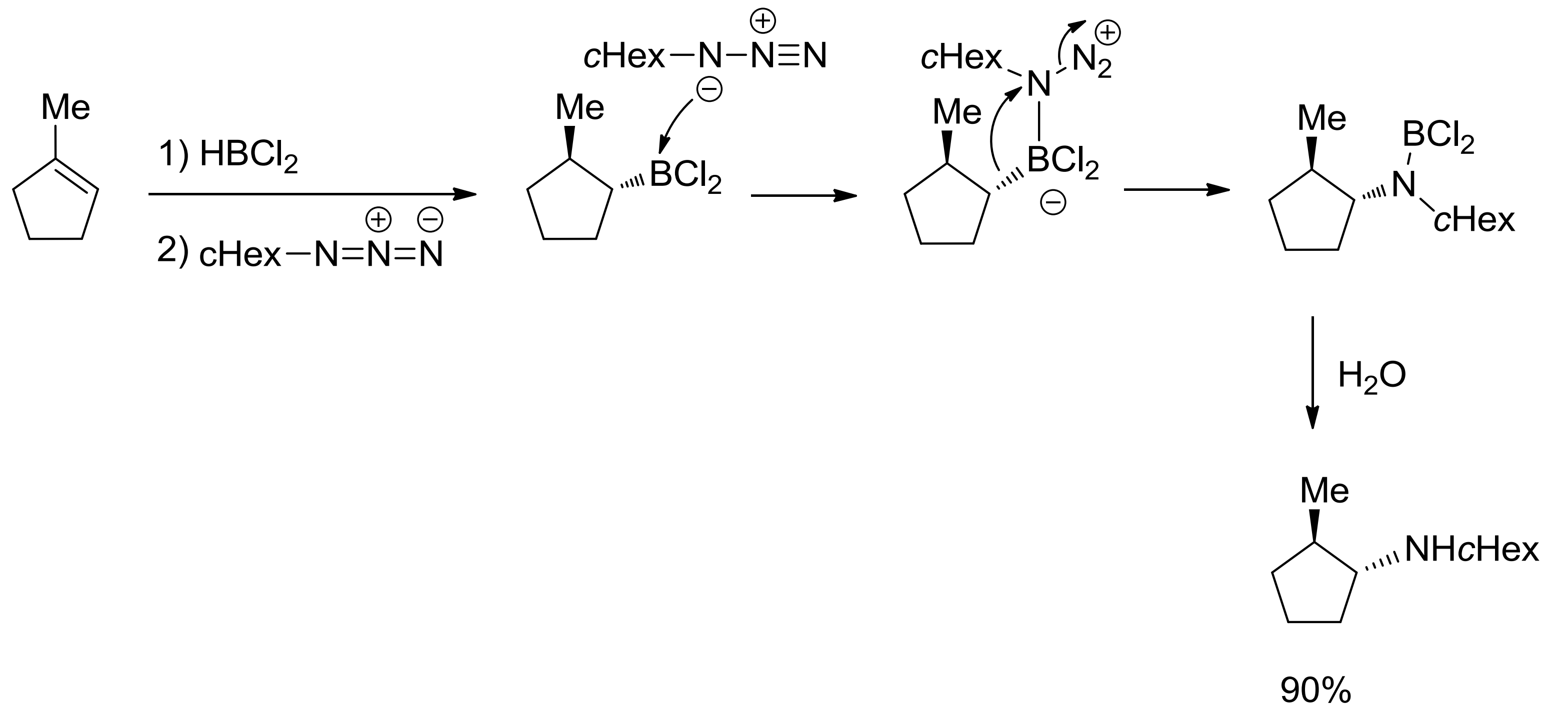
Rh$^+$ cat., -35 °C

90%; 93% ee

S. Demay, M. Lotz, P. Knochel *Tetrahedron: Asymmetry* **2001**, *12*, 909

Hydroboration

amination

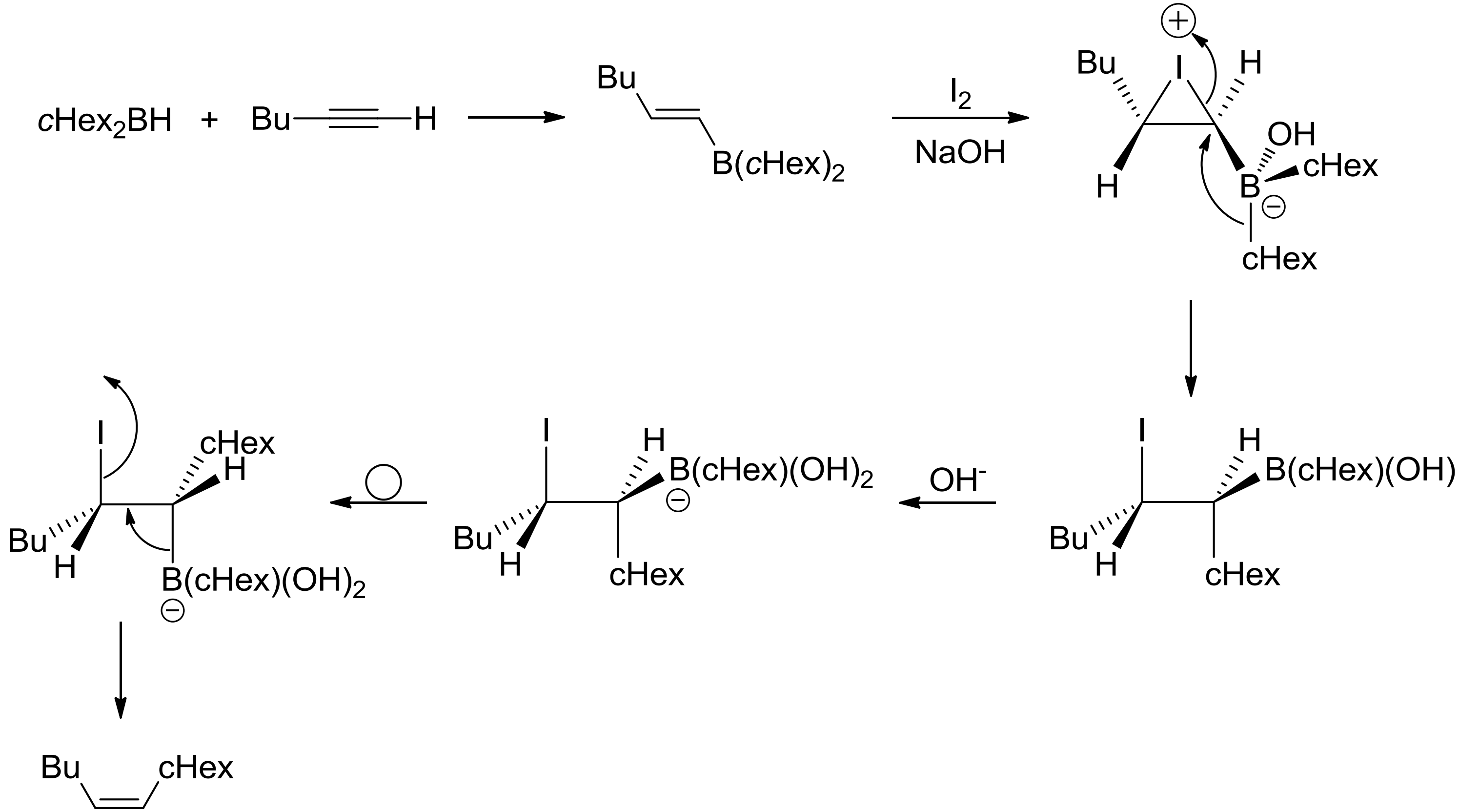


H. C. Brown, et al. *Tetrahedron* **1987**, *43*, 4079

Hydroboration

stereoselective synthesis of olefins

Z-olefins

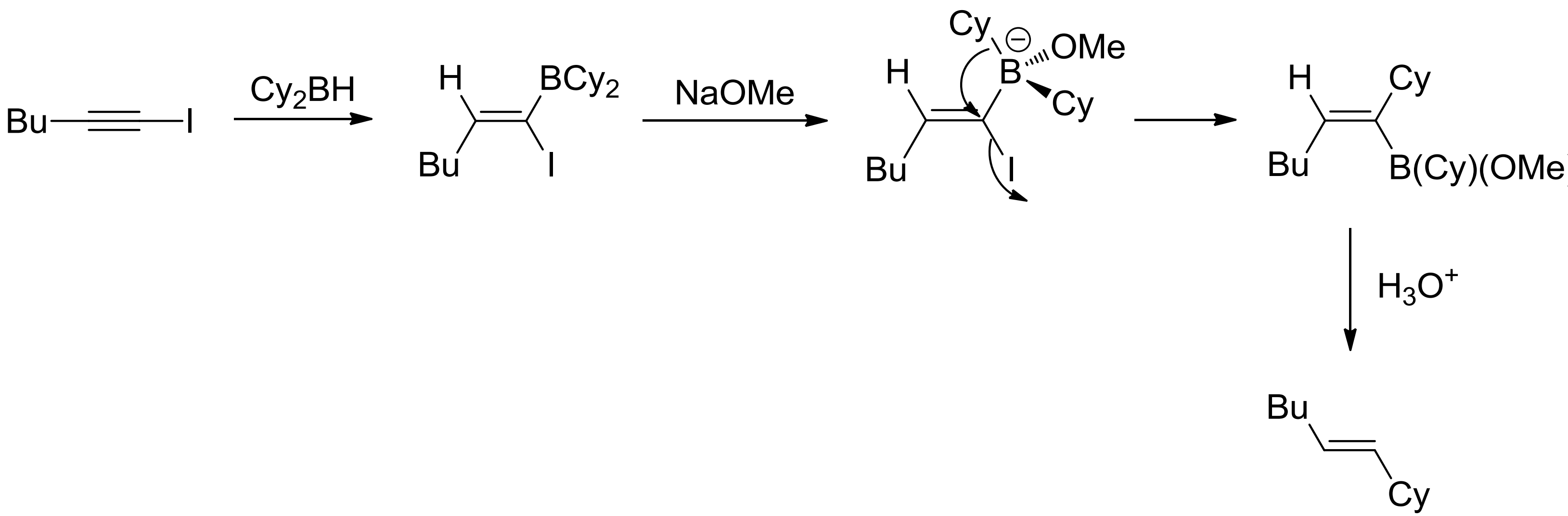


G. Zweifel, et al. *J. Am. Chem. Soc*. **1972**, *94*, 6560.

Hydroboration

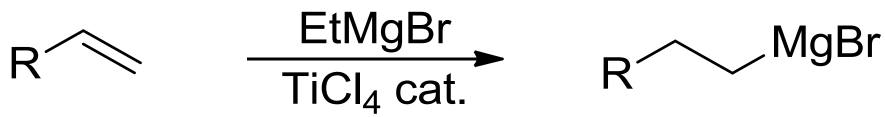
stereoselective synthesis of olefins

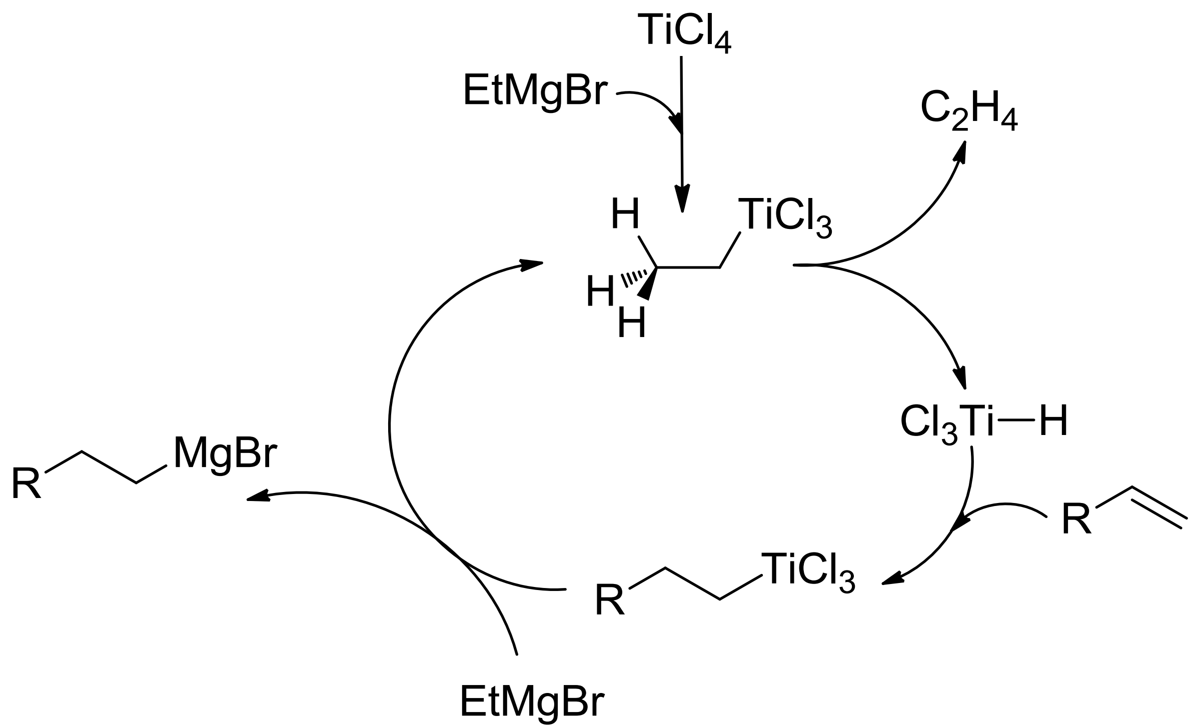
E-olefins



H. C. Brown, et al *J. Org. Chem*. **1989**, *54*, 6064.

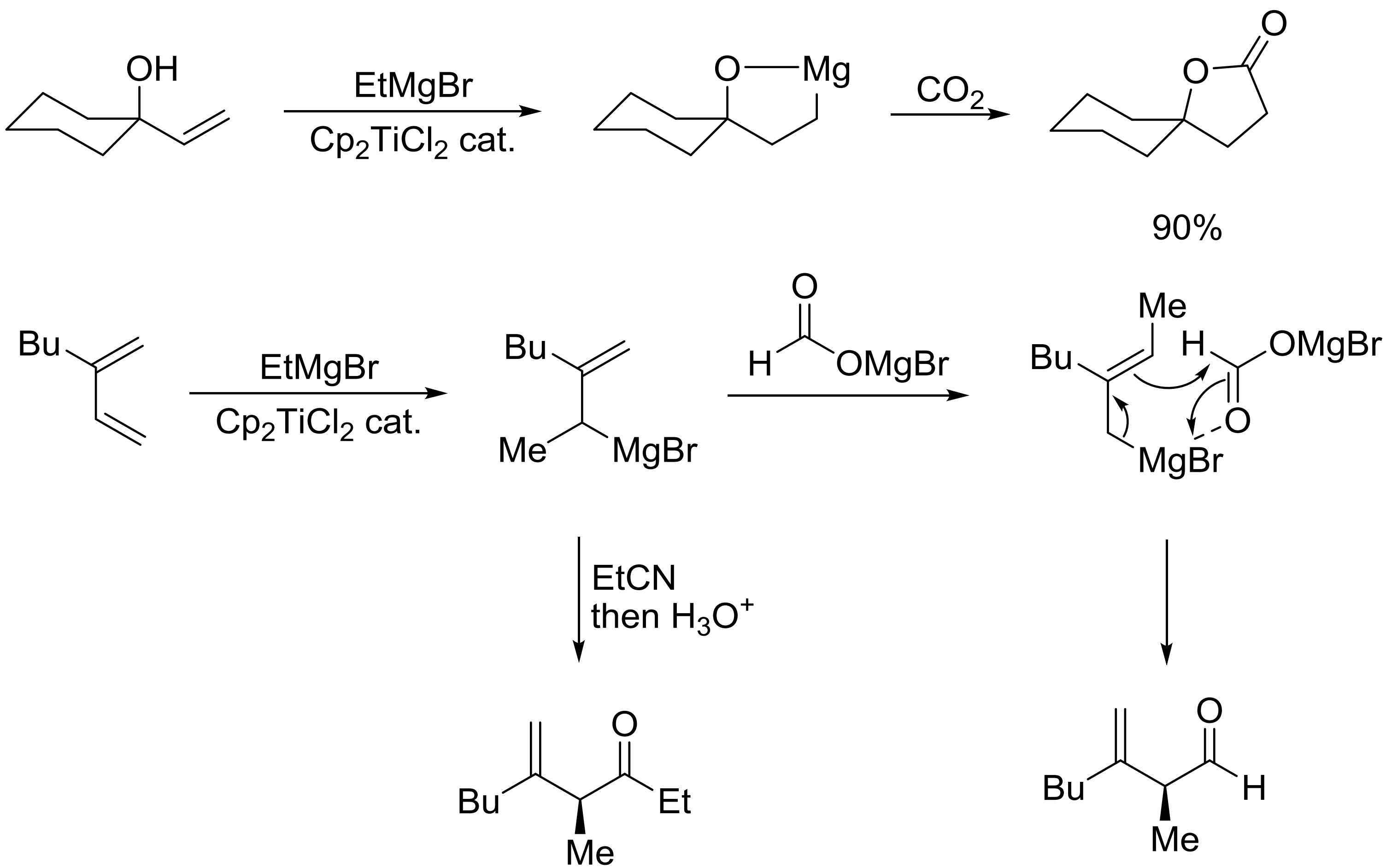
Hydromagnesiation





F. Sato, *Chem. Rev*. **2000**, *100*, 2835; *Synlett* **2000**, 753

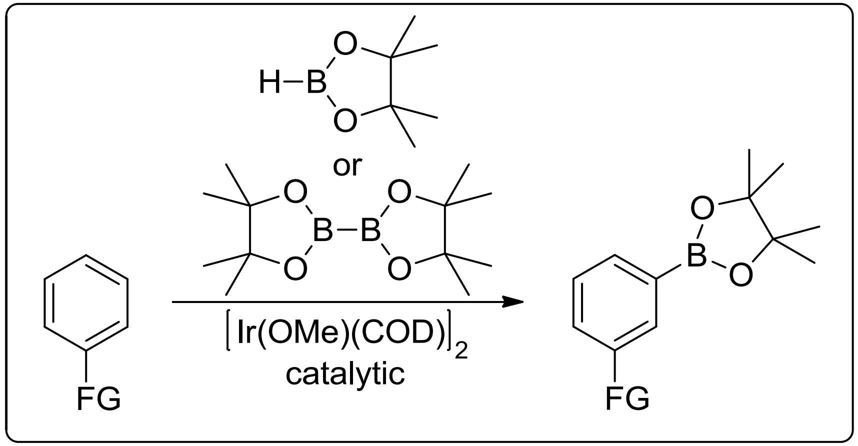
Hydromagnesiation

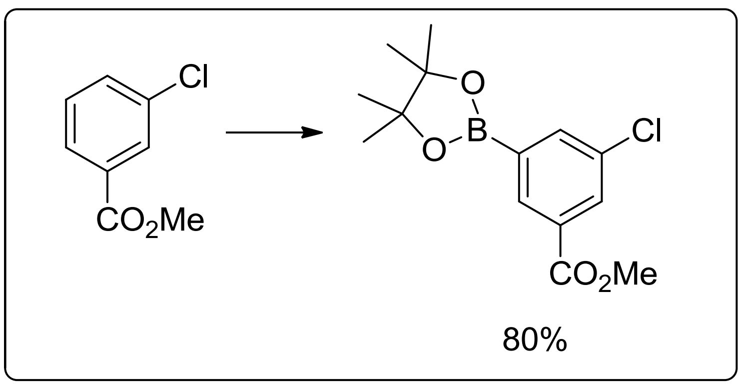


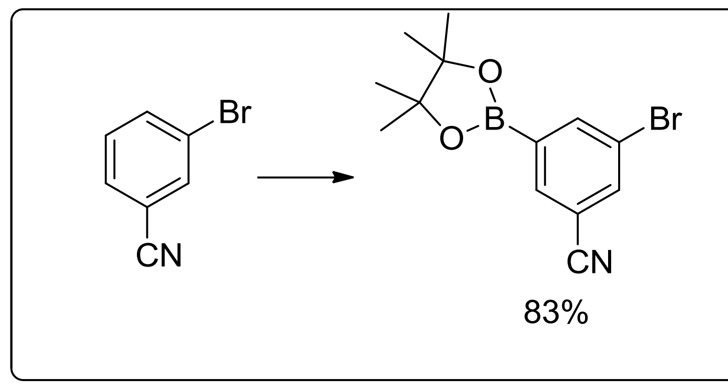
F. Sato, *Chem. Rev*. **2000**, *100*, 2835

Synthesis of aryl boronic acids

transition-metal catalyzed synthesis of aryl boronic acids

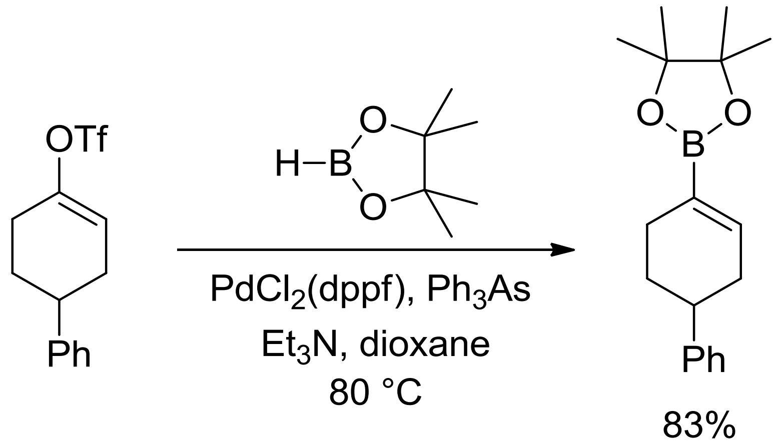




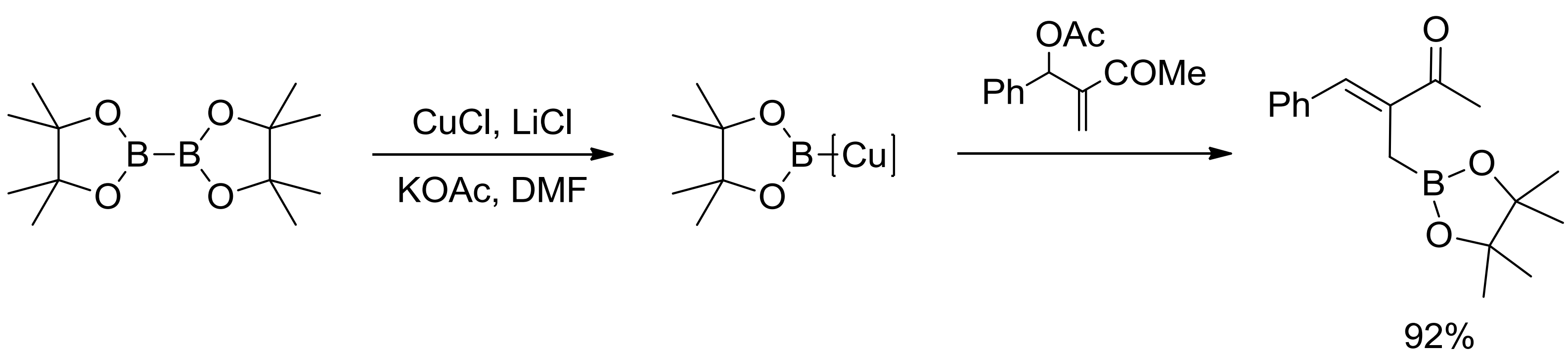


J. F. Hartwig, N. Miyaura, *Chem. Comm*. **2003**, 2924;
J. Am. Chem. Soc. **2002**, *124*, 390; *Angew. Chem. Int. Ed*. **2002**, *45*, 3056

Synthesis of aryl boronic acids



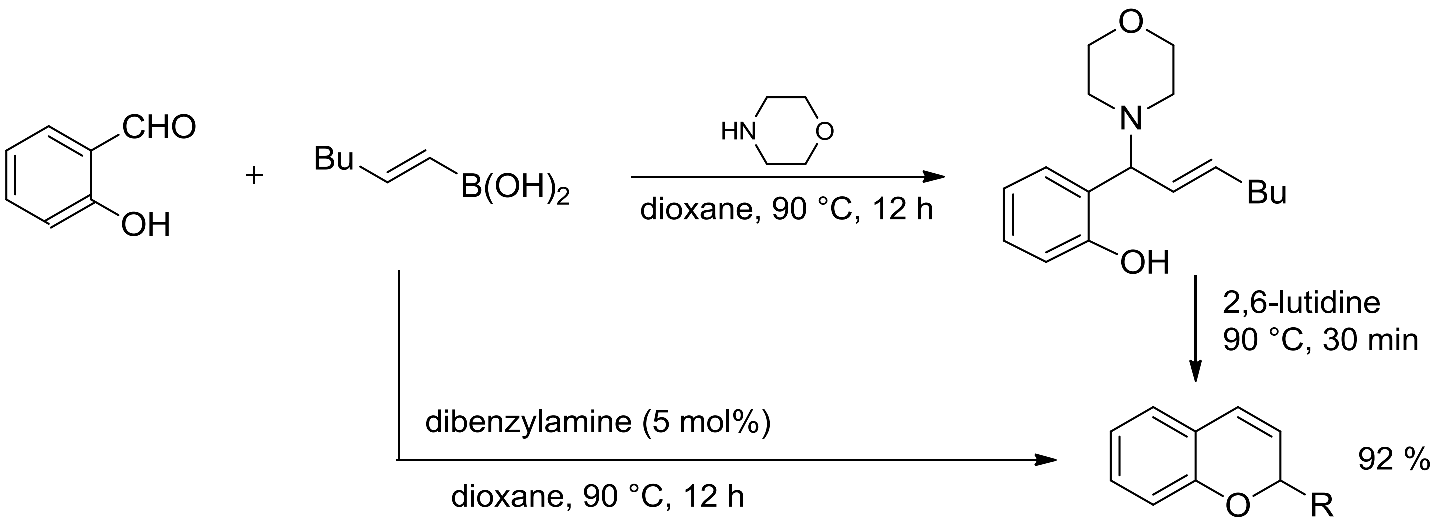
M. Murata *Tetrahedron Lett*. **2000**, *41*, 5877
M. Murata *Synth. Comm*. **2002**, *32*, 2513



P. V. Ramachandran *Org. Lett*. **2004**, *6*, 481

Reactivity of unsaturated boronic derivatives

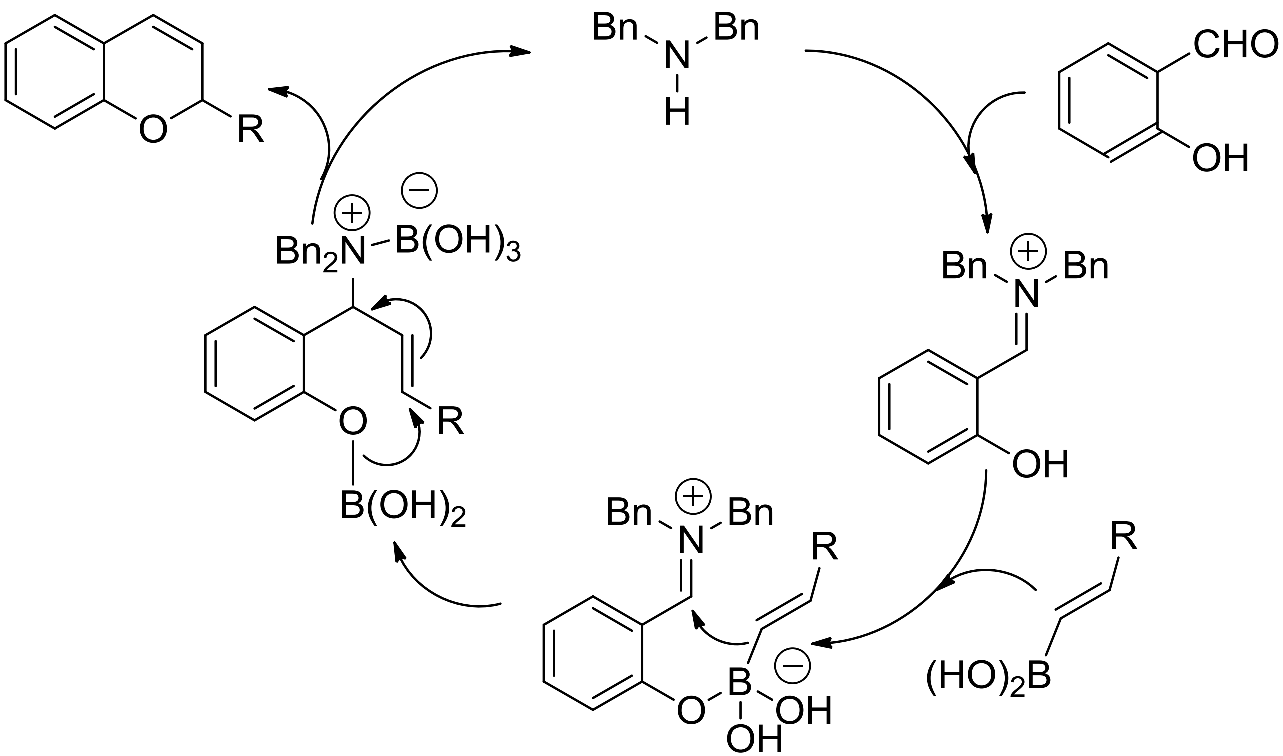
the Petasis-reaction - a short synthesis to 2H-chromenes



Reactivity of unsaturated boronic derivatives

The Petasis-reaction

mechanism



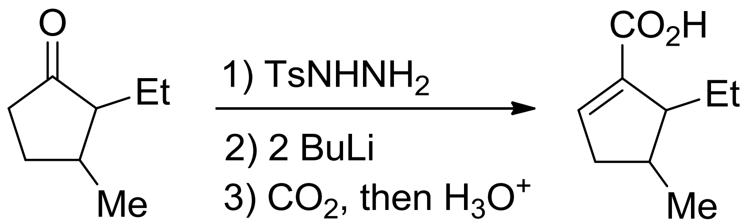
M. G. Finn, *Org. Lett*. **2000**, *2*, 4063

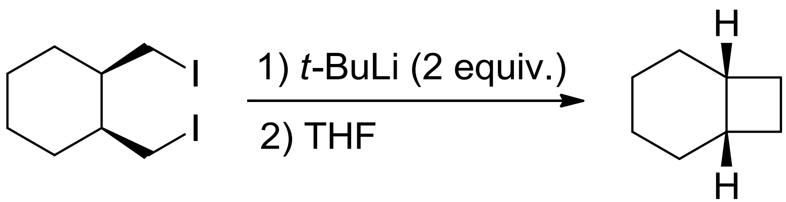
ÜBUNG

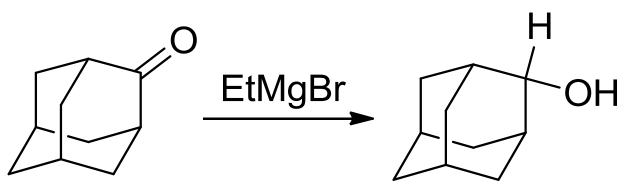
1. Problem set

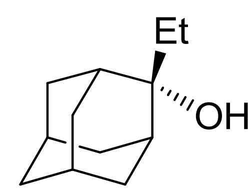
First Problem Set for OC IV

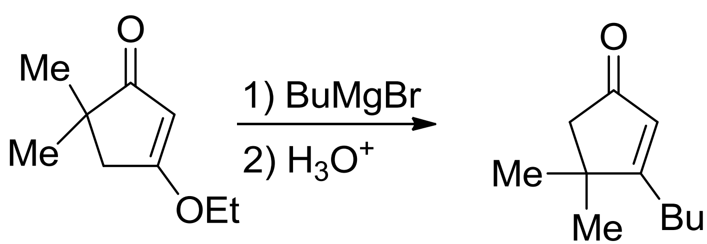
1) Give a mechanism for the following reactions:

a) 

b) 

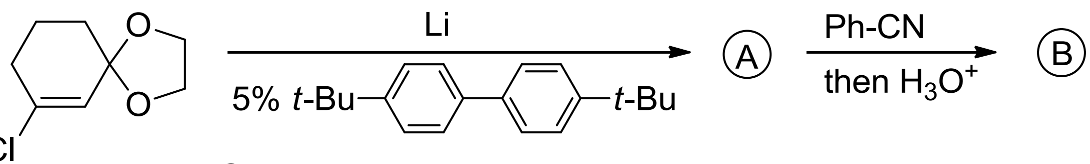
c) 

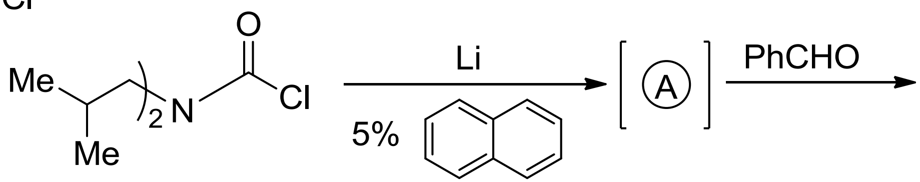
How would you prepare 

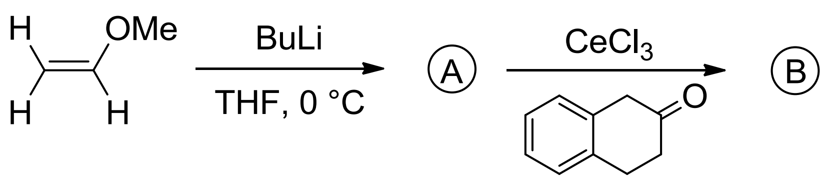
d) 

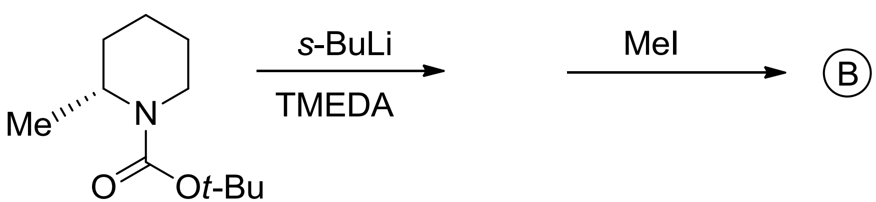
First Problem Set for OC IV

2) Give the following reaction products:

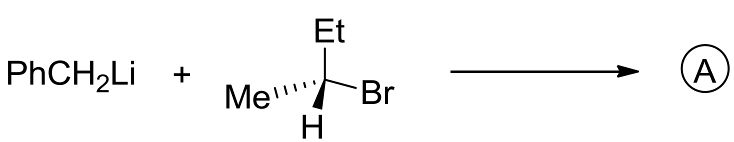
a)


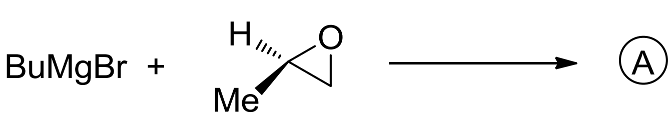
b)


c)


d)


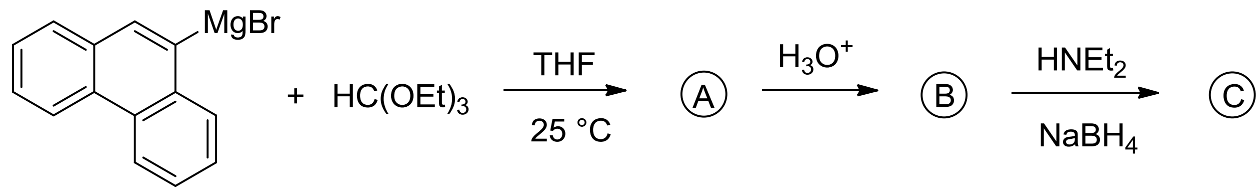
stereochemie?

e)


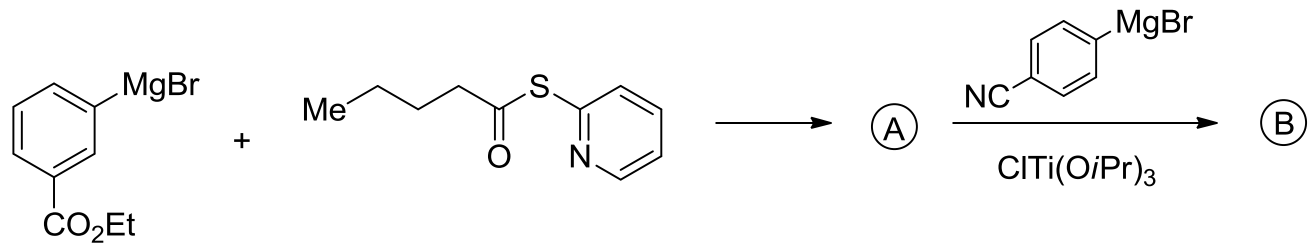
f)


First Problem Set for OC IV

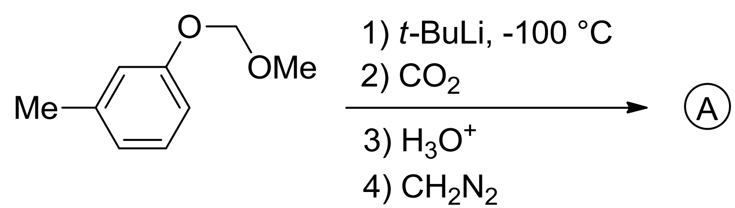
g)



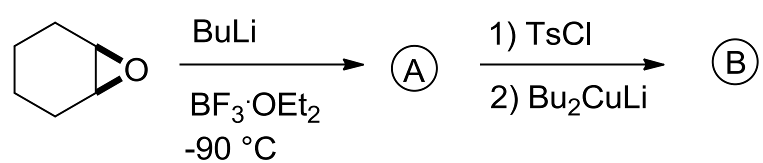
h)



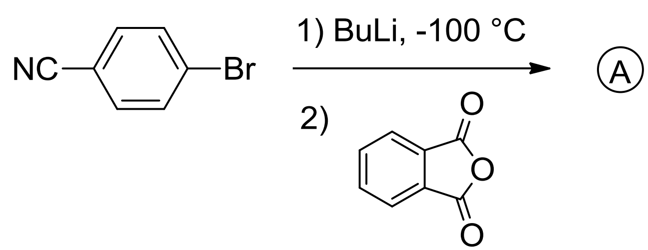
i)



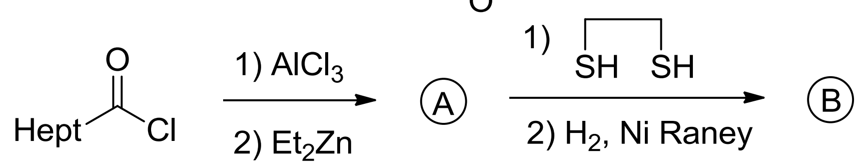
j)



k)

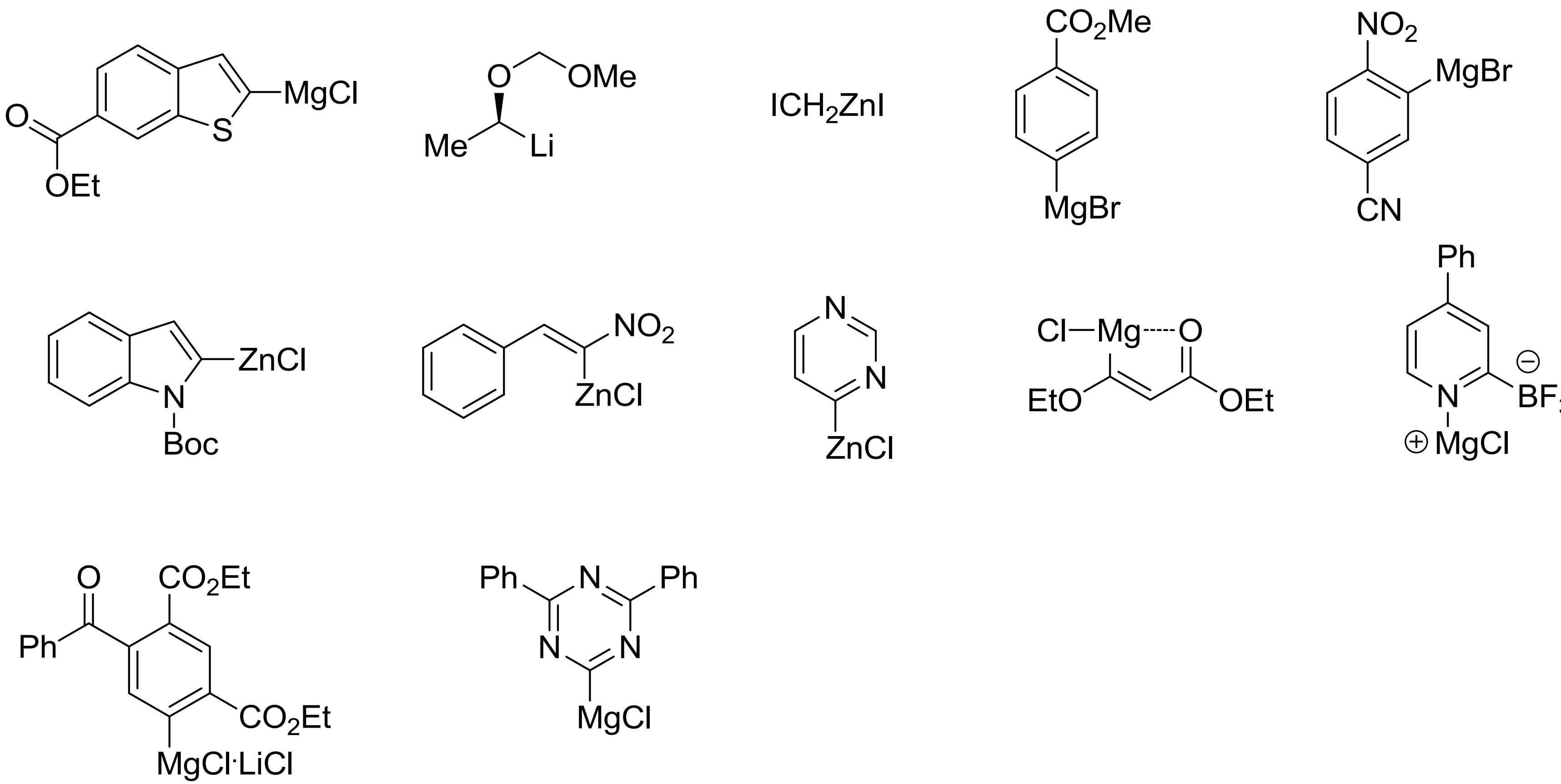


l)



First Problem Set for OC IV

3. How you would prepare following organometallics:

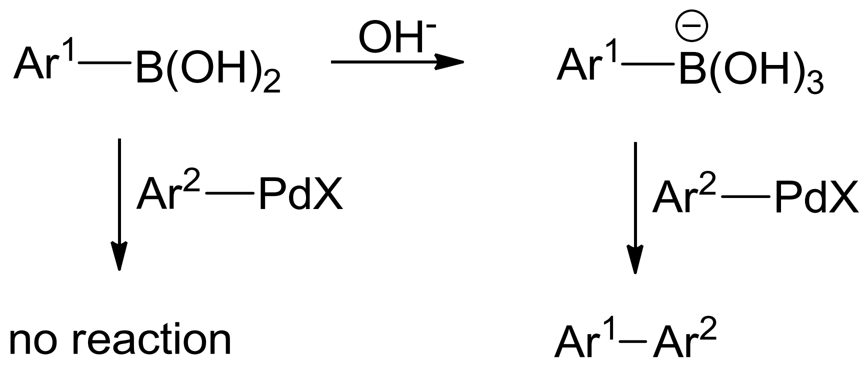


The Suzuki cross-coupling reaction

$$Ar^1{-}B(OH)_2 \quad + \quad Ar^2{-}X \xrightarrow[\text{base}]{\text{Pd(0) cat.}} Ar^1{-}Ar^2$$

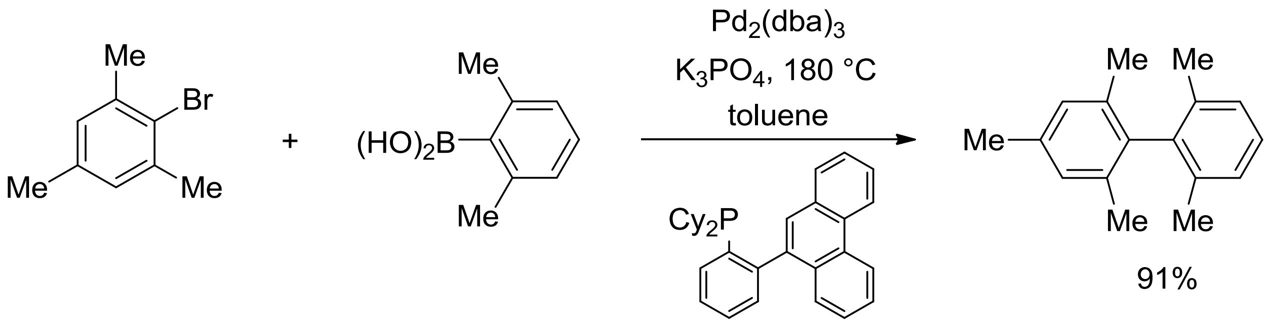
N. Miyaura, A. Suzuki *Chem. Rev*. **1995**, *95*, 2457
Cross-Coupling Reactions. A practical guide. N. Miyaura (Ed.), Springer, **2002**

Key step

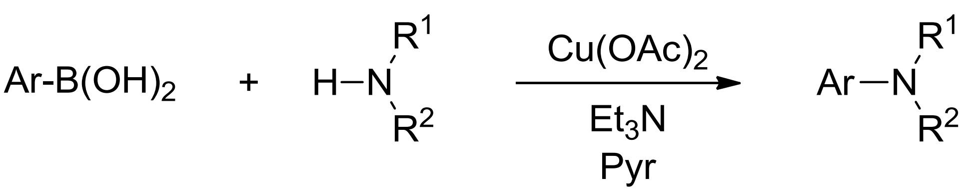


S. Buchwald, *J. Am. Chem. Soc*. **2002**, *124*, 1162
C. Amatore, A. Jutand, G. Le Duc *Chem. Eur. J*. **2011**, *17*, 2492
B. P. Carrow, J. F. Hartwig *J. Am. Chem. Soc*. **2011**, *133*, 2116

The Suzuki cross-coupling reaction

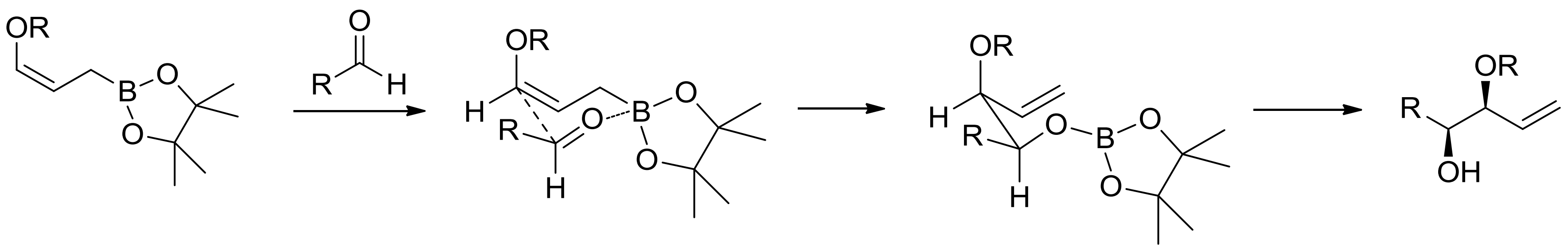


R. E. Sammelson, M. J. Kurth, *Chem. Rev*. **2001**, *101*, 137



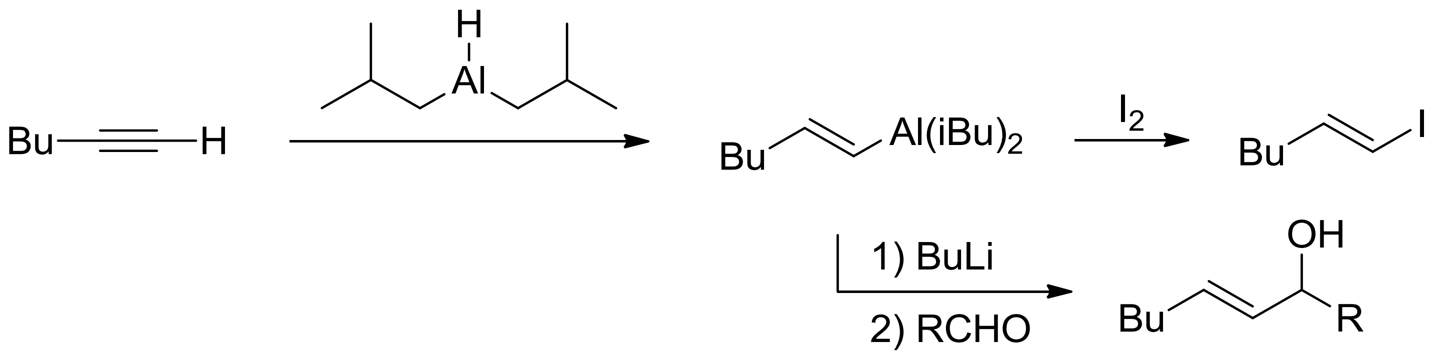
D. A. Evans, *Tetrahedron Lett*. **1998**, *39*, 2937
S. Ley, *Angew. Chem. Int. Ed*. **2003**, *42*, 5400

Chemistry of allyl boranes



R. W. Hoffmann, *Tetrahedron* **1984**, *40*, 2219

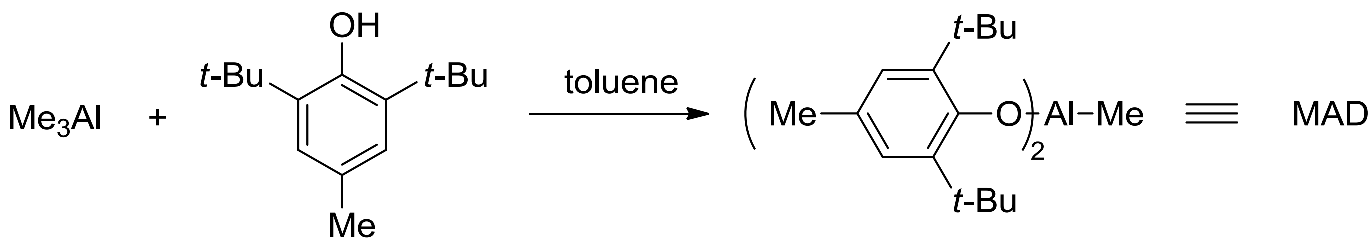
Hydroalumination

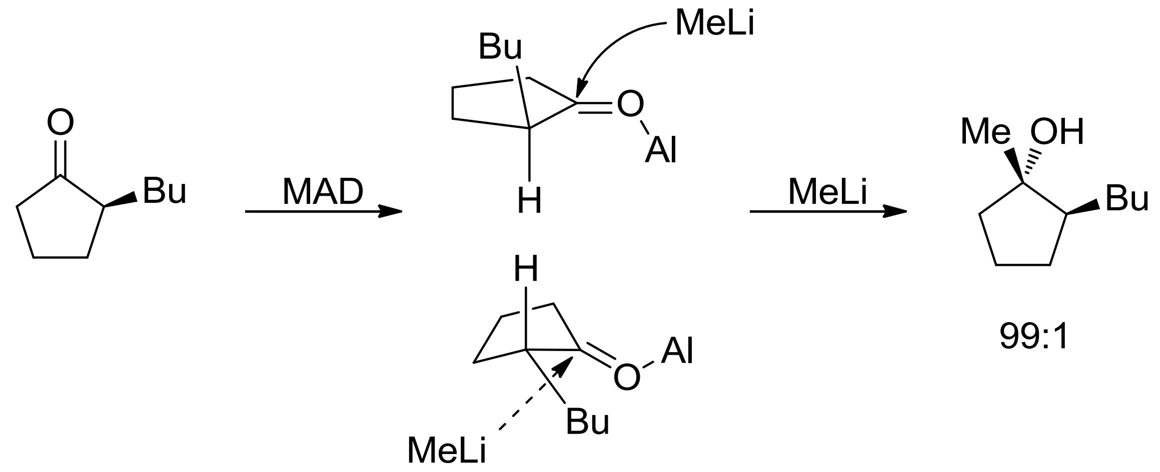


G. Zweifel, *Org. React*. **1984**, *32*, 375

Hydroalumination

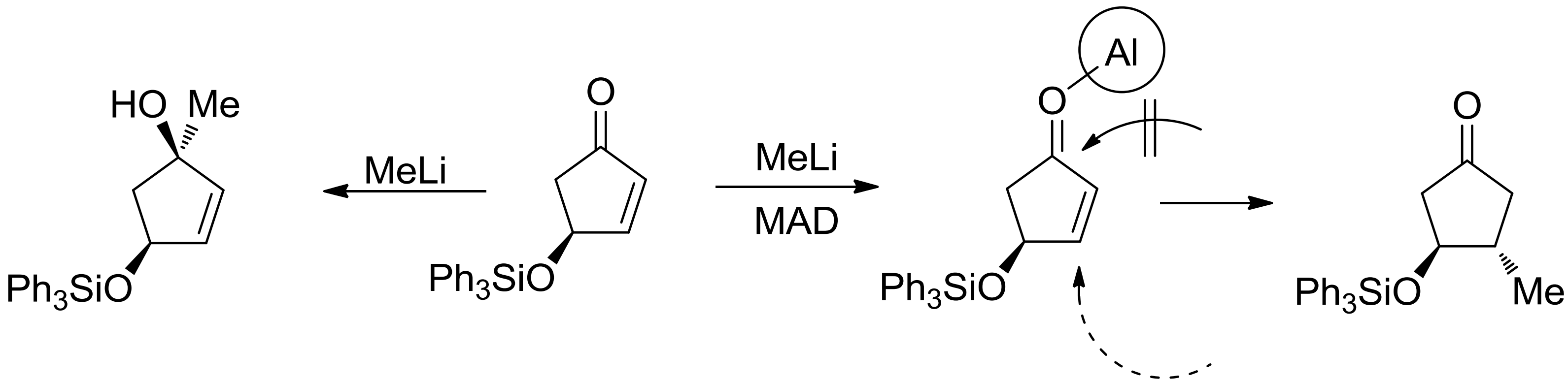
Special Al-reagents

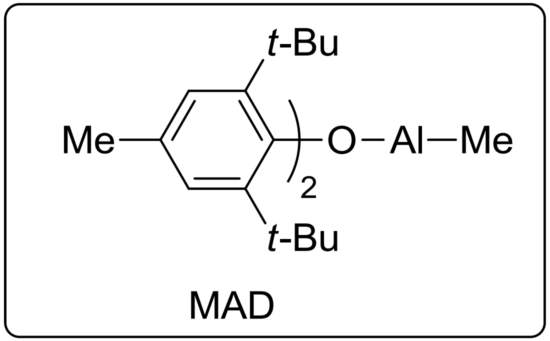




H. Yamamoto *J. Am. Chem. Soc*. **1988**, *110*, 3588
H. Yamamoto *Chem. Comm*. **1997**, 1585

Hydroalumination



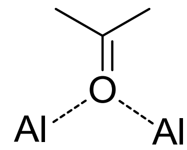


K. Maruoka, H. Yamamoto, Kagaku, Zokan (Kyoto, Japan) **1988**, *115*, 127
S. Nagahara, K. Maruoka, H. Yamamoto, *Bull Chem Soc*. **1993**, *66*, 3783

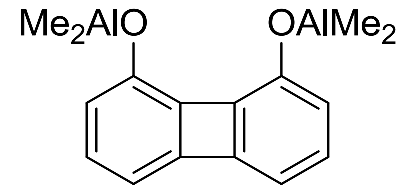
Hydroalumination

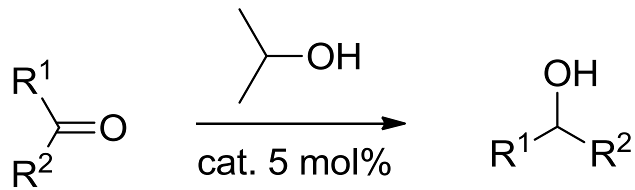
Verley-Meerwein-Ponndorf reduction

activating a carbonyl group twice

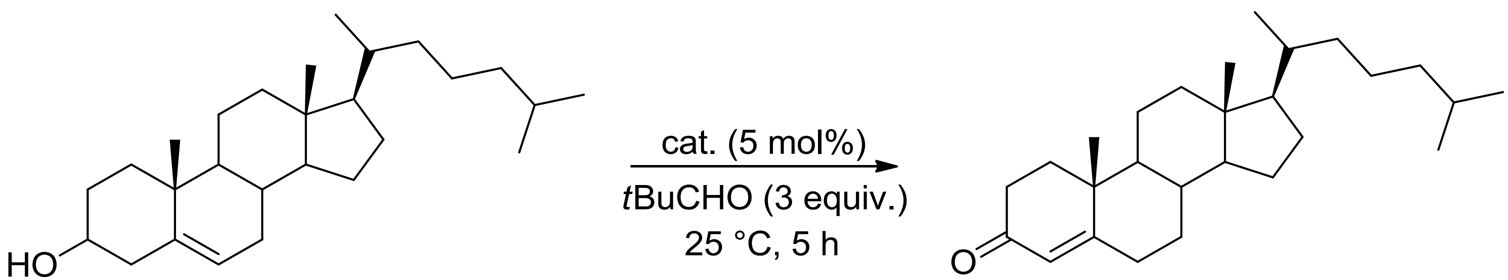


is possible using



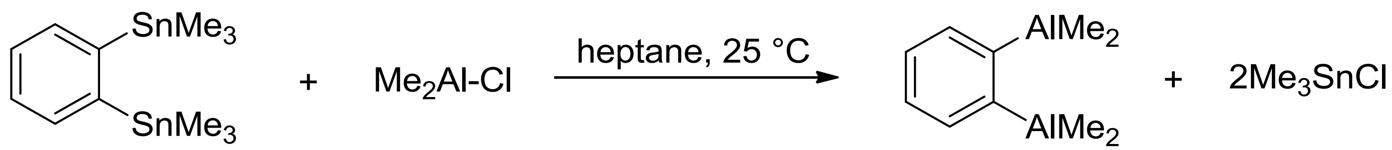


80 - 99%



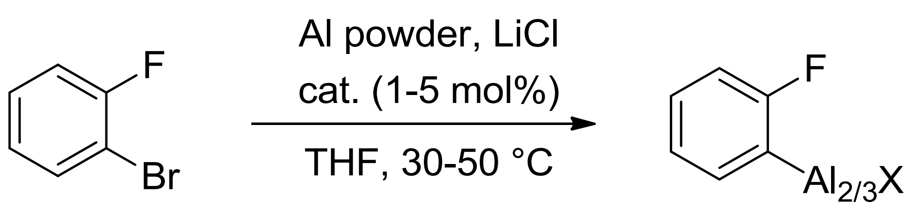
K. Maruoka *Angew. Chem*. **1998**, *110*, 2524

Other preparation of aluminium compounds



K. Dimroth, *Angew. Chem. Int. Ed*. **1964**, *3*, 385

Direct synthesis of organoaluminium reagents

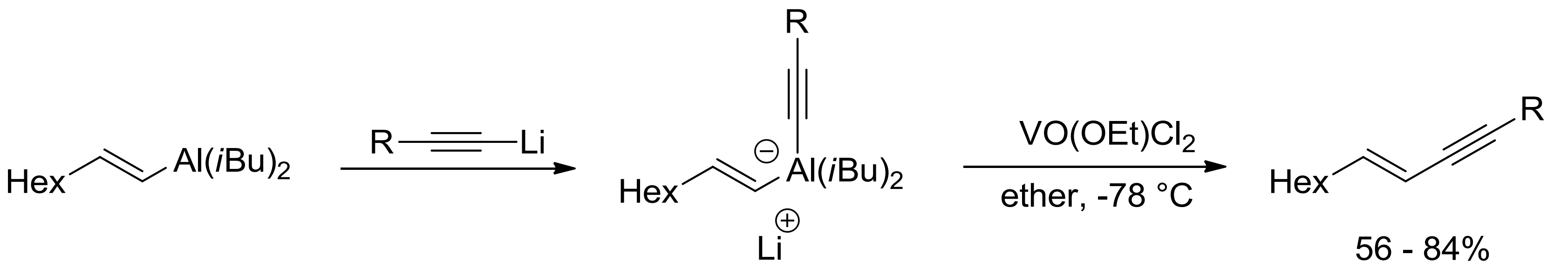


cat. = $InCl_3$, $BiCl_3$, $PbCl_2$, $TiCl_4$

T. Blümke, Y.-H. Chen, Z. Peng, *Nature Chem*. **2010**, *2*, 313

Hydroalumination

Reactivity



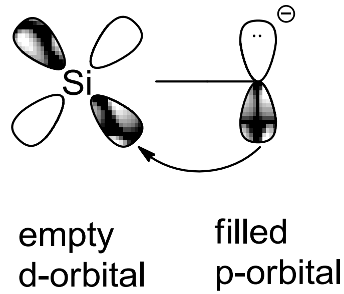
T. Ishikawa, A. Ogawa, T. Hirao *J. Am. Chem. Soc*. **1998**, *120*, 5124

The organic chemistry of main-group organometallics

Silicium

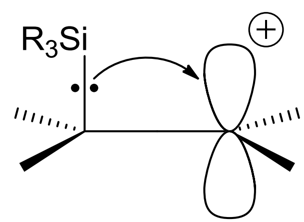
The effect of a Me_3Si-substituent:

1) inductive effect: weak donor-effect
2) retrodonation of π-electrons (d-p bond)



stabilization of carbanions in α-position

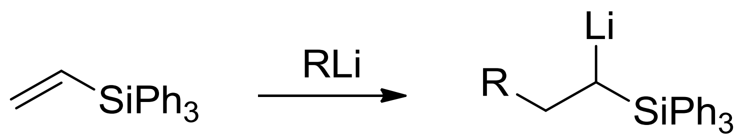
3) hyperconjugation: interaction of σ-framework with the π-system

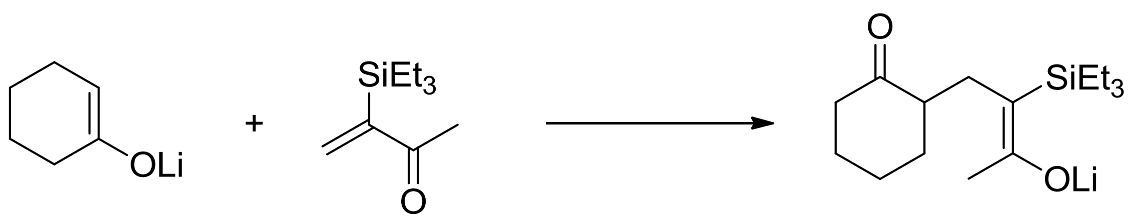


stabilization of a cation in β-position

Silicium

Applications:



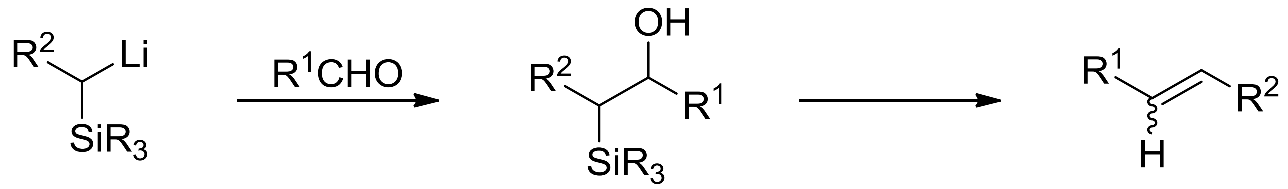


high yield: stabilized lithium enolate
(no polymerization)

G. Stork *J. Am. Chem. Soc*. **1973**, *95*, 6152; **1974**, *96*, 6181

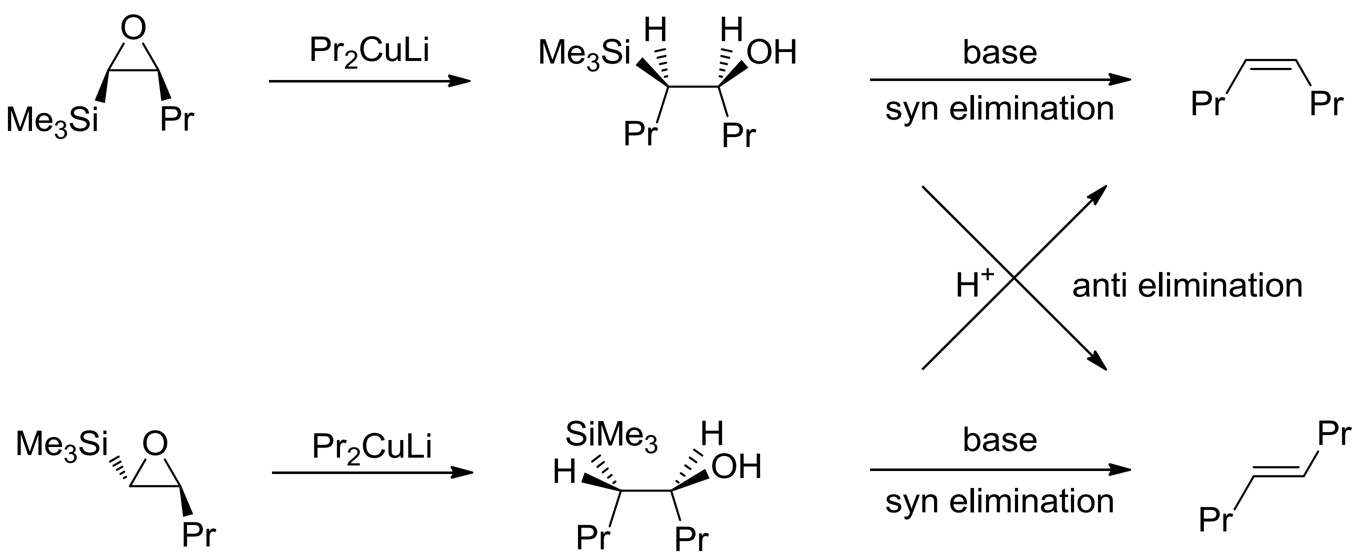
Silicium

Peterson olefination



D. J. Ager *Synthesis* **1984**, 384

Stereochemistry of the *Peterson*-elimination

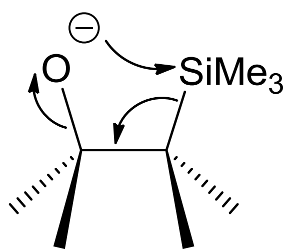


P. F. Hudrlik, D. Peterson, R. J. Rona *J. Org. Chem*. **1975**, *40*, 2263

Silicium

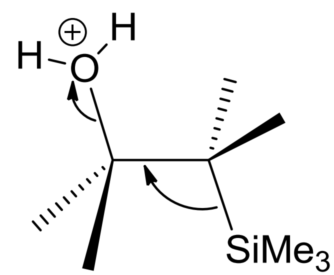
key steps:

basic media



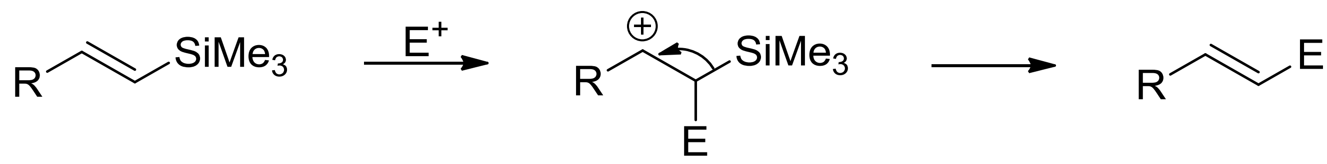
syn elimination

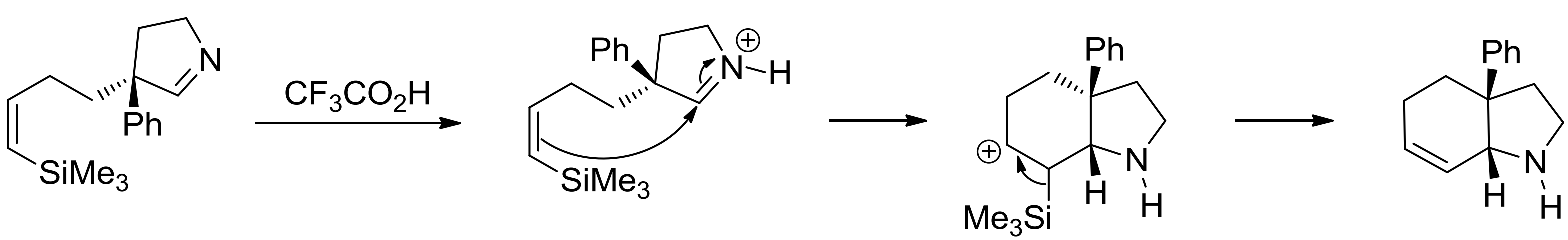
acidic media



anti elimination

Reactivity of alkenylsilanes

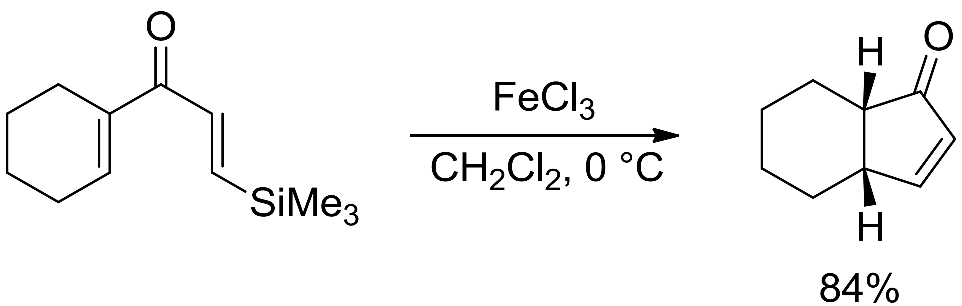




L. E. Overman, *Tetrahedron Lett*. **1984**, *25*, 5739

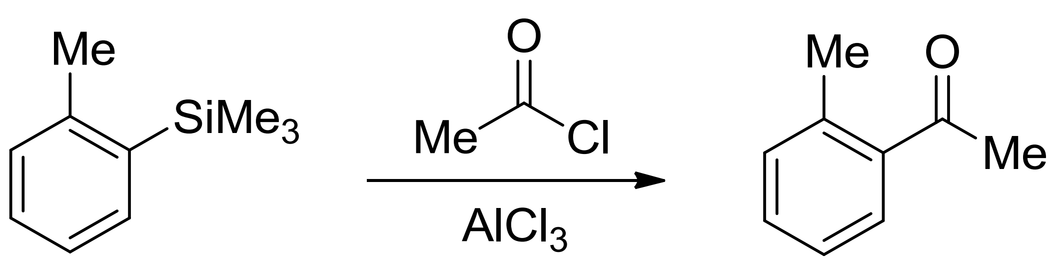
Reactivity of alkenylsilanes

Sila-Nazarov-reaction



S. E. Denmark *J. Am. Chem. Soc*. **1982**, *104*, 2642

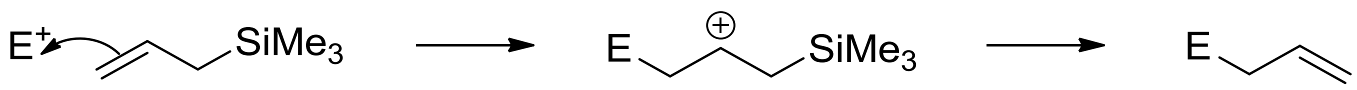
Aromatic ipso-substitution



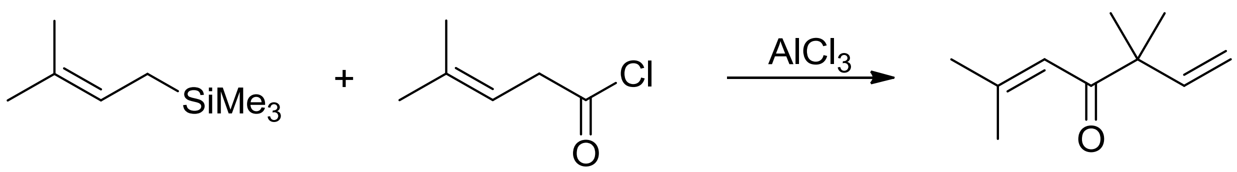
The reaction with $ArSnMe_3$ is 10^4 time faster

Allylic silanes in organic synthesis

General reactivity

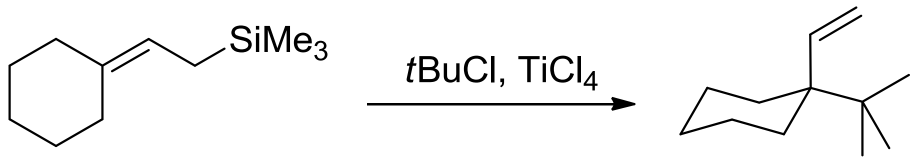


Acylation

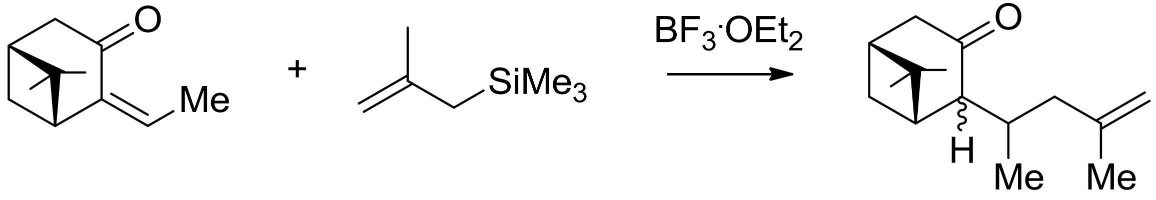


Allylic silanes in organic synthesis

Allylation



1,4-addition



T. Yanami, M. Miyashita, A. Yoshikoshi, *J. Chem. Soc. Chem. Commun*. **1979**, 525.
T. Yanami, M. Miyashita, A. Yoshikoshi, *J. Org. Chem*. **1980**, *45*, 607.

Indium

Element	Cost in Euro/Mol
In	167 Euro/Mol
Mg	1,5 Euro/Mol
Zn	3 Euro/Mol
Li	10 Euro/Mol

$$\mathrm{In} \xrightarrow[\text{SET}]{-\,e^{\ominus}} \mathrm{In}^{\oplus}$$

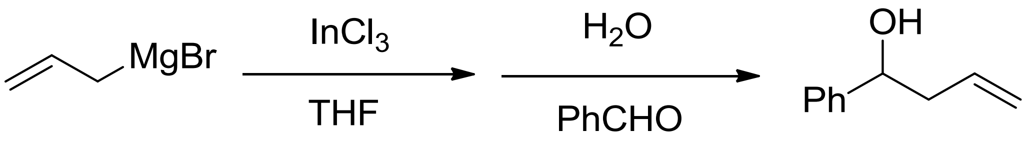
strong oxophilicity

The first ionization potential of indium (5,8 eV)
is close to lithium and sodium

Key contributions:

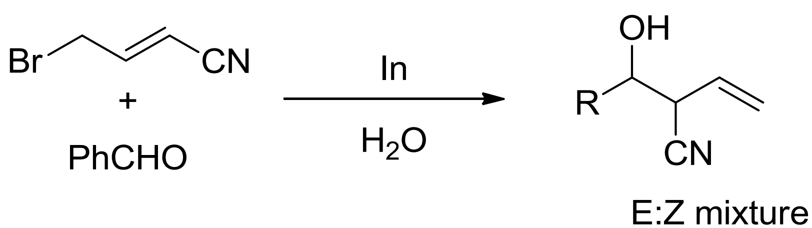
S. Araki *Main Group Metals in Organic Synthesis* **2004**, *1*, 323
T.-P. Loh *Acid Catalysis in Modern Organic Synthesis* **2008**, *1*, 377

Indium. Allylation reactions



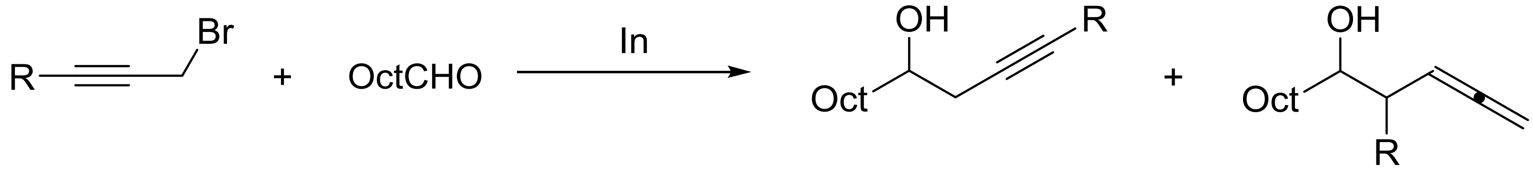
with H_2O: 73%
without H_2O: 98%

S. Akira, *J. Chem. Soc. Perkin Trans. I*, **1991**, 2395

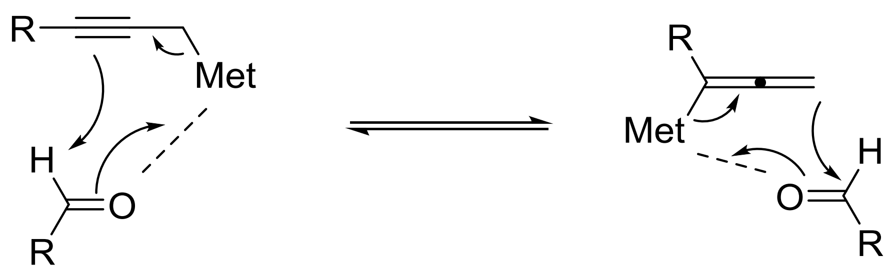


B. Manze, *Synth. Commun*. **1996**, *26*, 3179

Indium



1 **2**



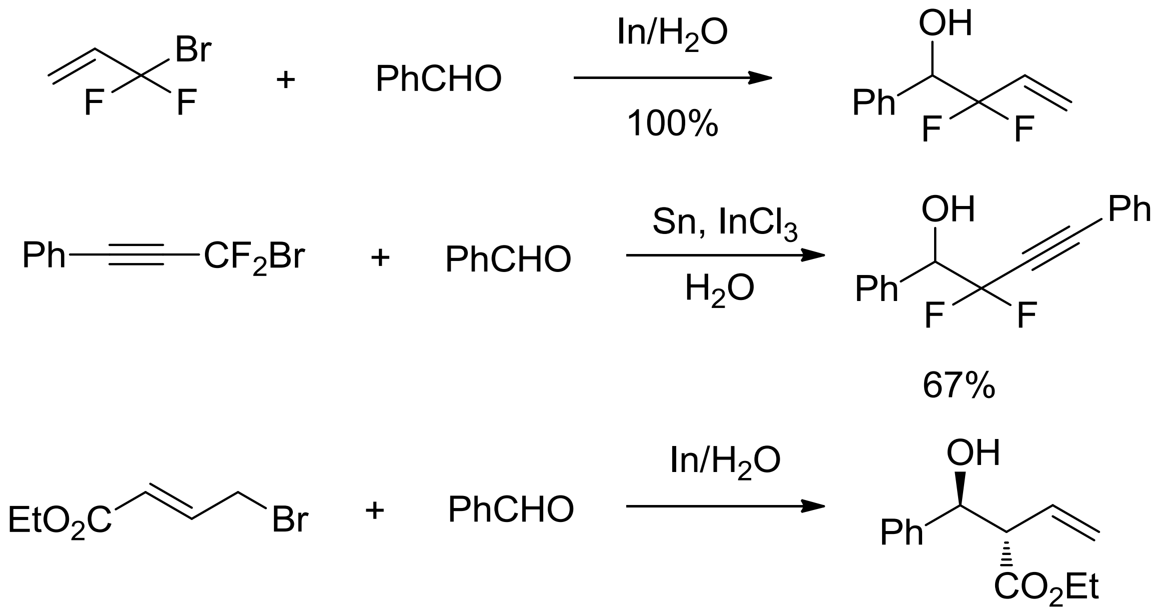
allenyl alcohol

propargylic alcohol

R	Conditions	Yield	Ratio **1** : **2**
Me_3Si	THF, InF_3 (10 mol%)	93	99:1
iPr_3Si	THF:H_2O (1:5)	52	5:95

T. P. Loh, *J. Am. Chem. Soc*. **2003**, *125*, 13042

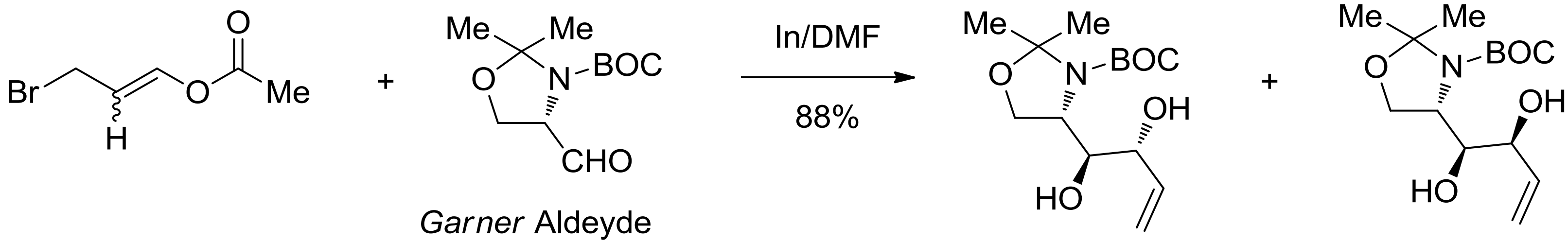
Indium



without $La(OTf)_3$: 59% anti:syn = 86 : 14
with $La(OTf)_3$: 99% anti:syn = 90 : 10

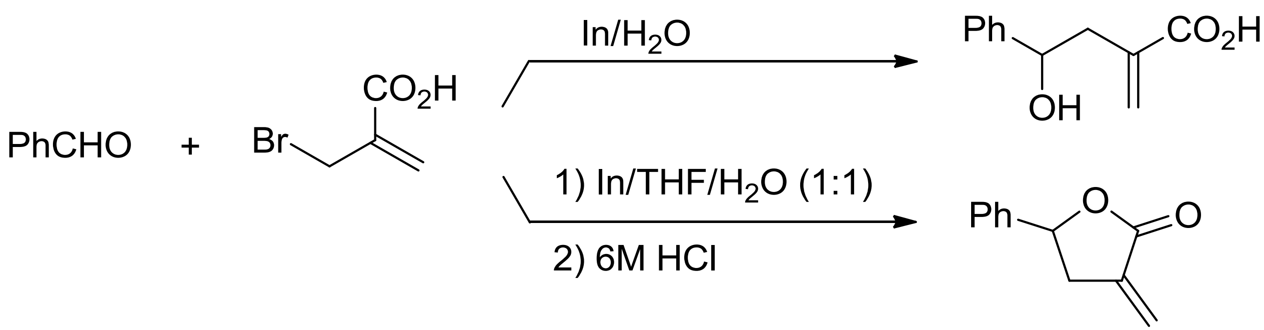
L. A. Paquette, *Tetrahedron Lett*. **1999**, *40*, 4129

Indium



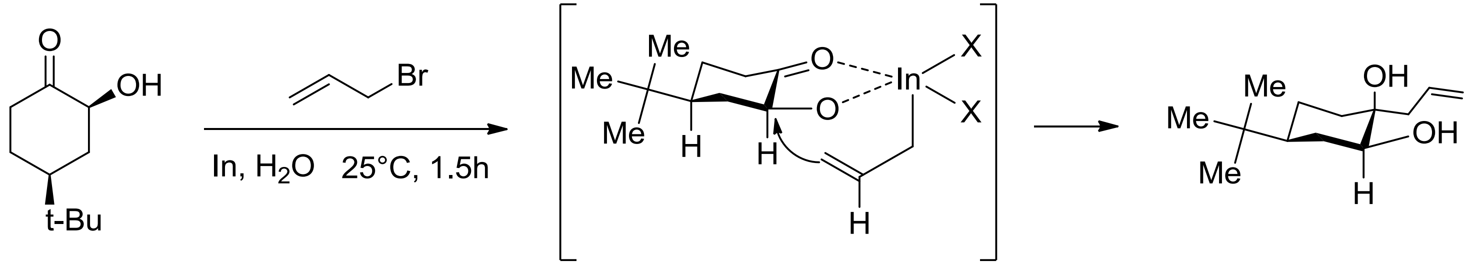
97 : 3

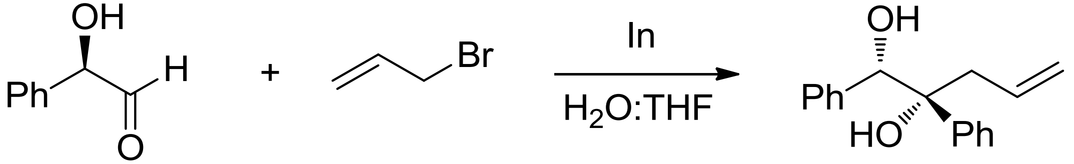
M. Lombardo, *Pure Appl. Chem*. **2004**, *76*, 657



T. H. Chan, *J. Org. Chem*. **1995**, *60*, 4228

Indium



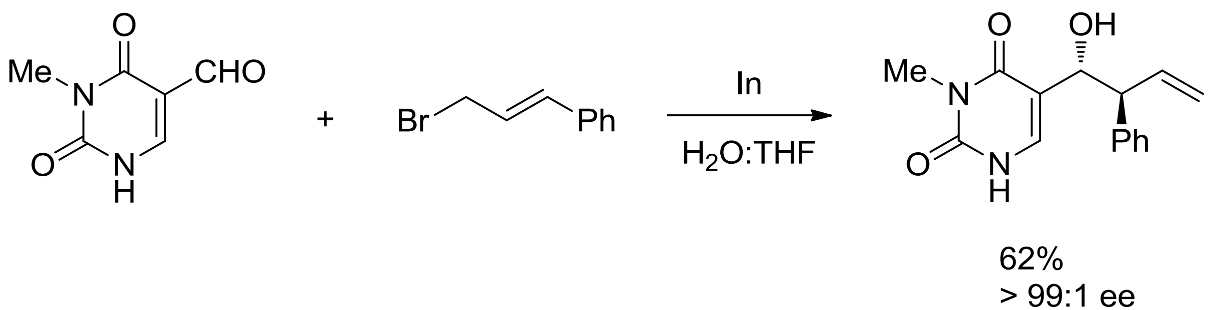


90%
> 98% ee

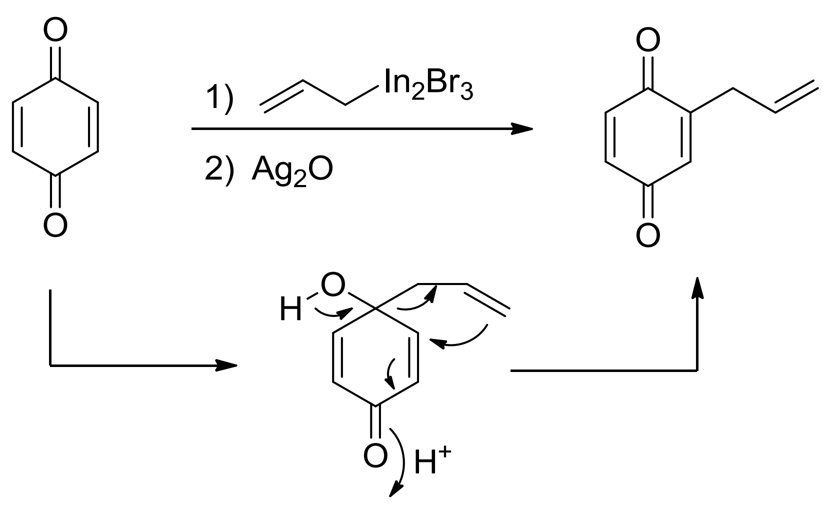
L. A. Paquette, *Org. Lett*. **2000**, *2*, 1263

Indium

Applications in nucleoside chemistry:

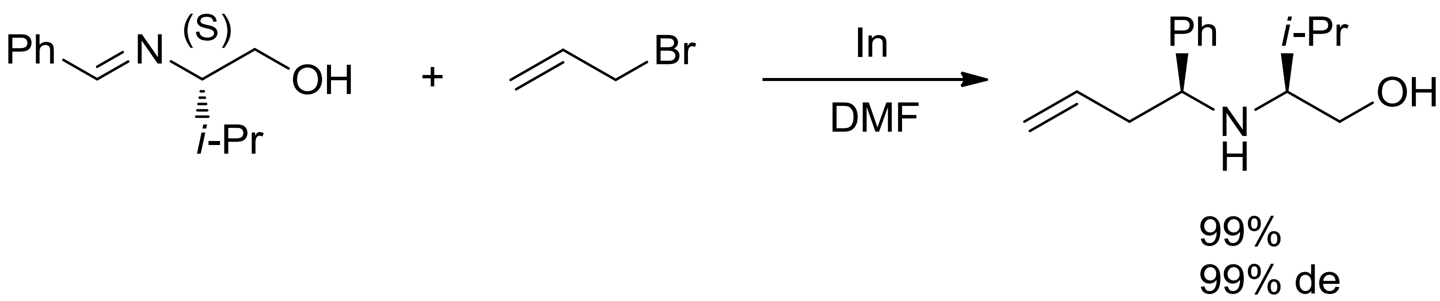


S. Kumar, *Tetrahedron Lett*. **2001**, *42*, 7039

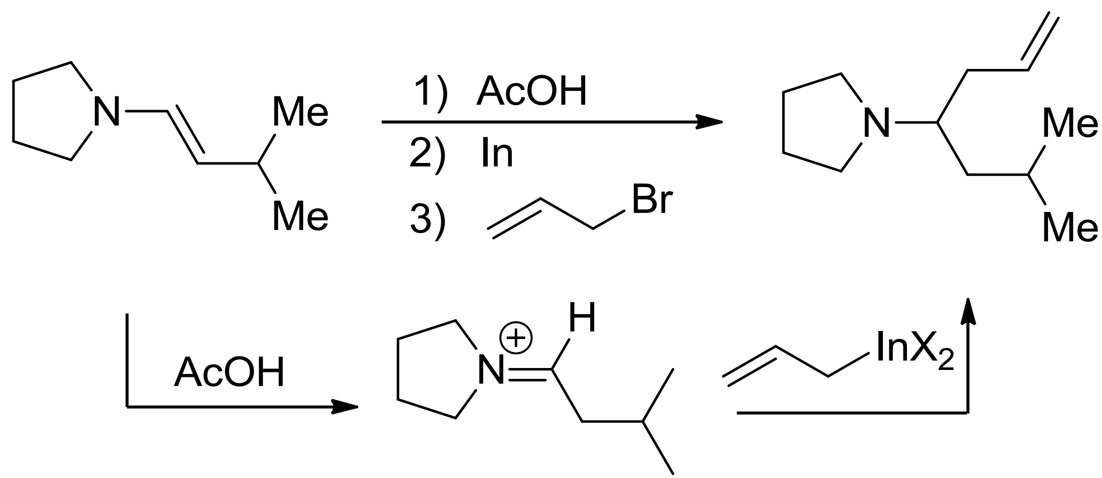


S. Akiva, *J. Organomet. Chem*. **1991**, *415*, 7

Indium



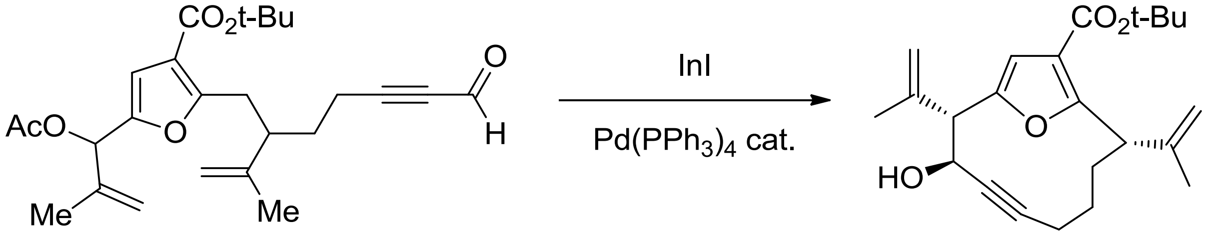
T. P. Loh, *Tetrahedron Lett*. **1997**, *38*, 865



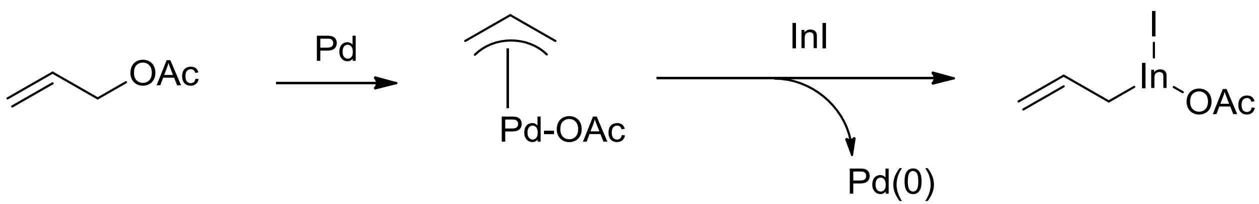
P. Mosset *Tetrahedron Lett*. **1995**, *36*, 6055
P. Mosset *Chem. Eur. J*. **1997**, *3*, 1064

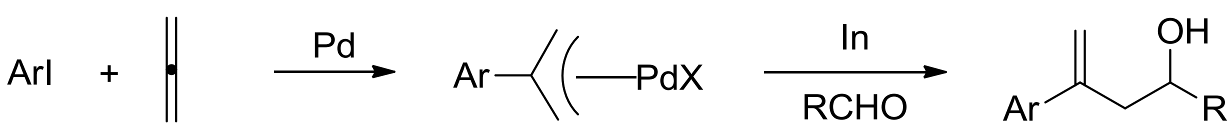
Indium

Applications in natural product syntheses:



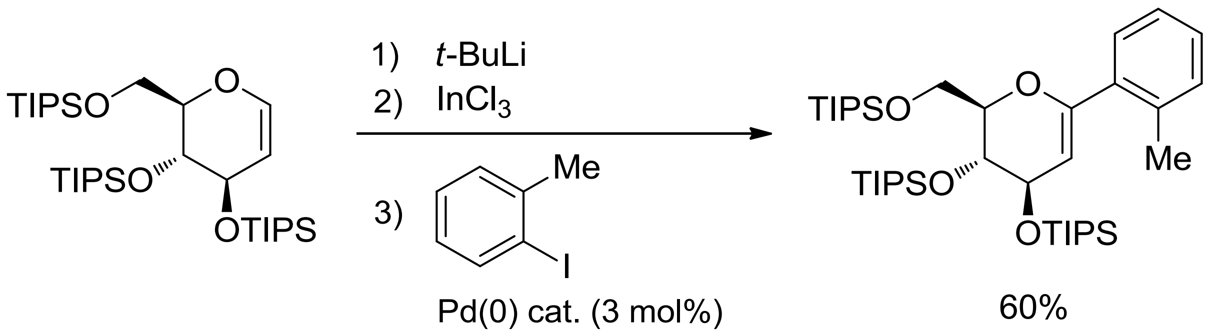
J. A. Marshall, *J. Org. Chem*. **1999**, *64*, 5193





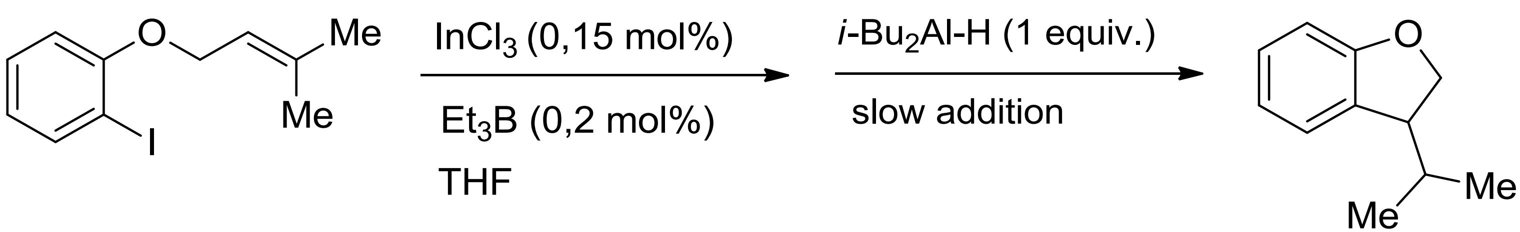
S-K. Kang S-W. Lee J. Jung Y. Lim *J. Org. Chem*. **2002**, *67*, 4376

Indium



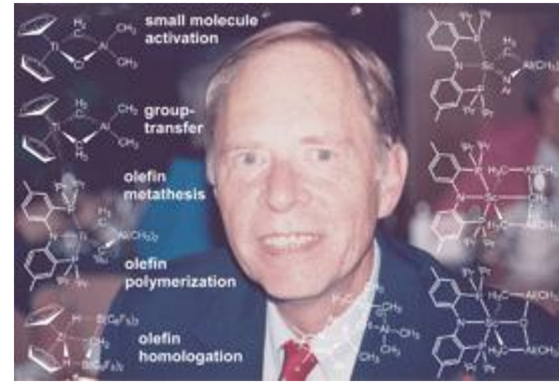
U. Lehmann, *Org. Lett*. **2003**, 5, 2405

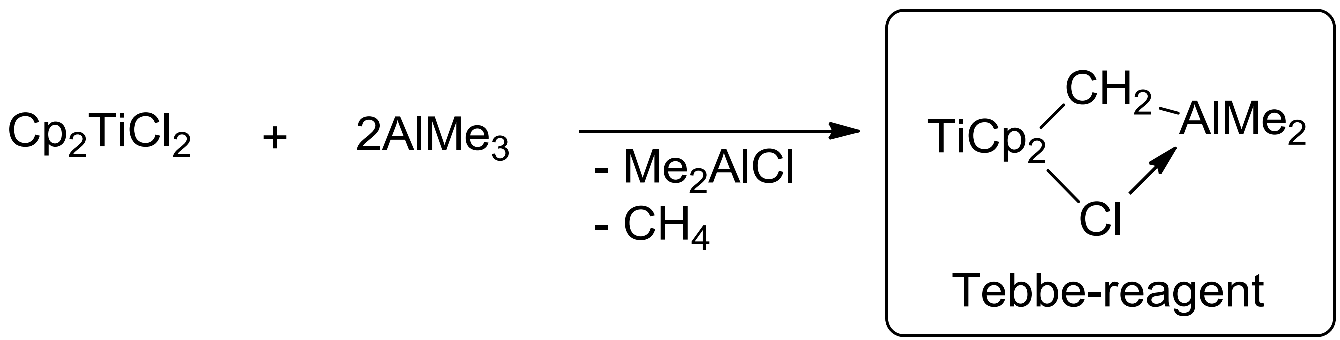
radical reaction

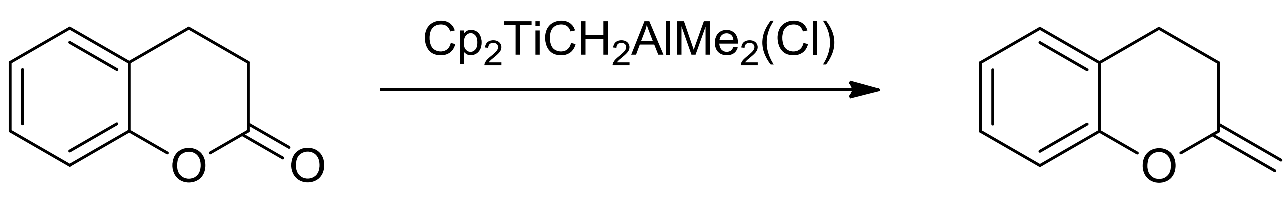


K. Oshima, *Tetrahedron*, **2003**, *59*, 6627

Early transition metal organometallics: Titanium



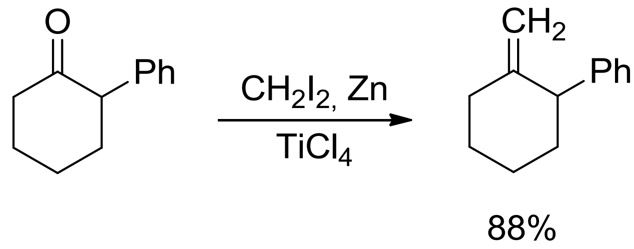




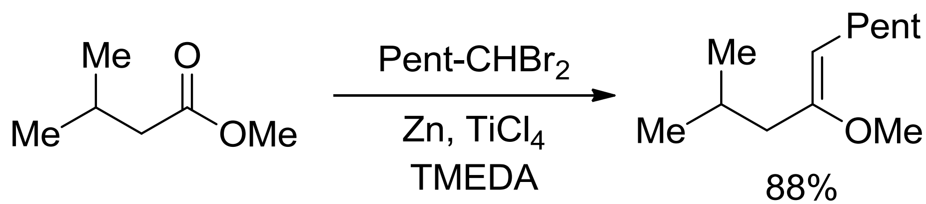
S. H. Pine *Org. React*. **1993**, *43*, 1

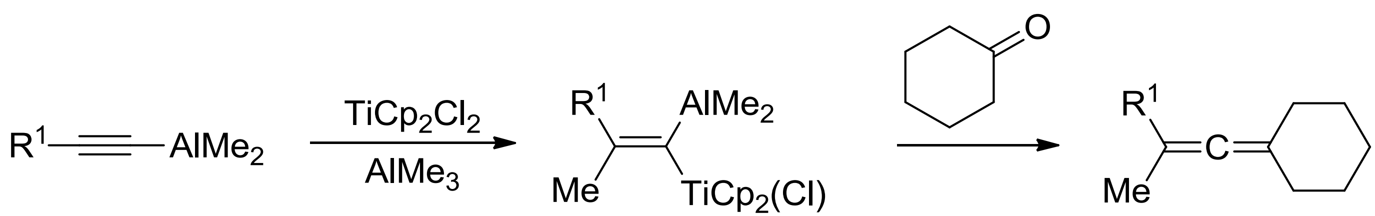
Titanium

Lombardo-reagent



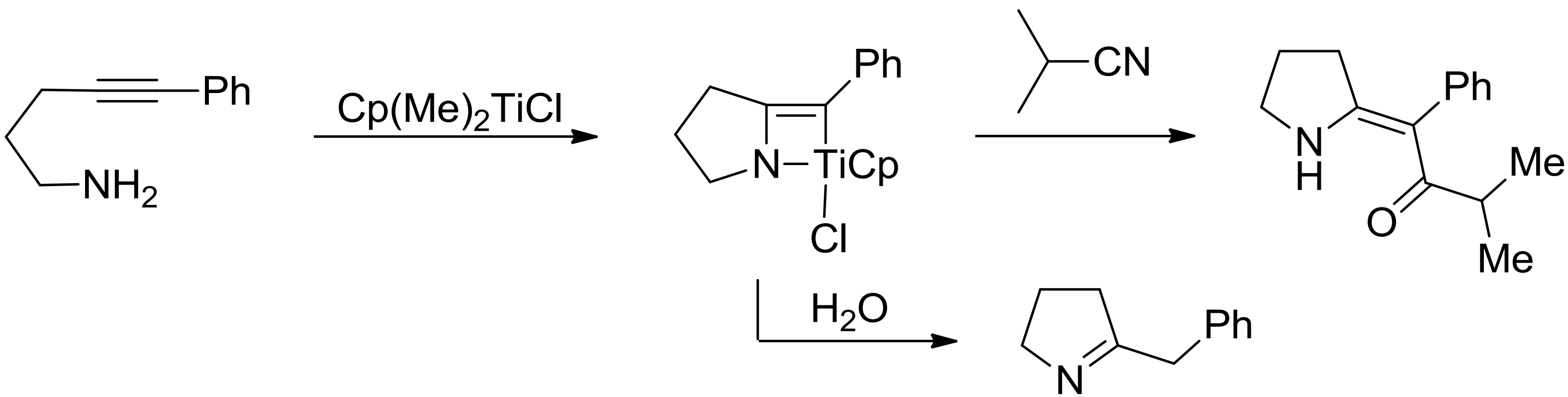
K. Takai, *J. Org. Chem*. **1994**, *59*, 2668





S. Buchwald, R. H. Grubbs *J. Am. Chem. Soc*. **1983**, *105*, 5490

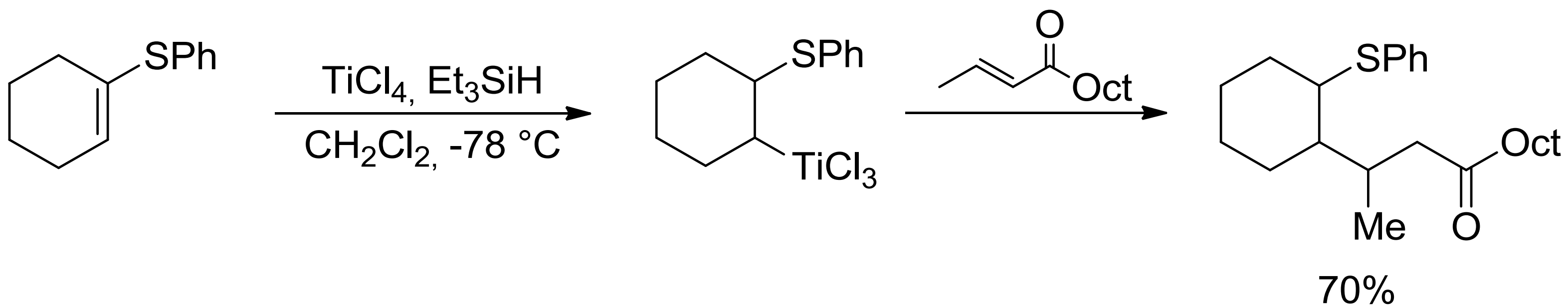
Titanium



T. Livinghouse, *J. Am. Chem. Soc*. **1992**, *114*, 5459

Titanium

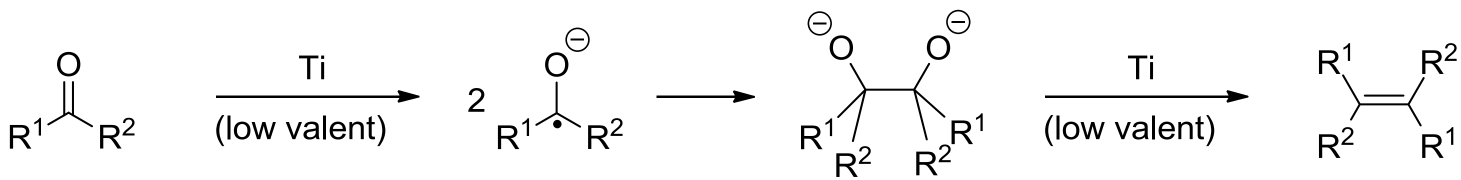
Hydrotitanation

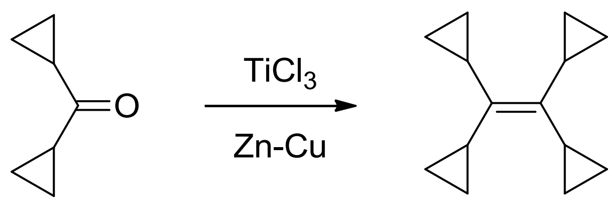


T. Takeda, *Tetrahedron Lett*. **1985**, *26*, 5313

Titanium

Reductive coupling: The McMurry Reaction

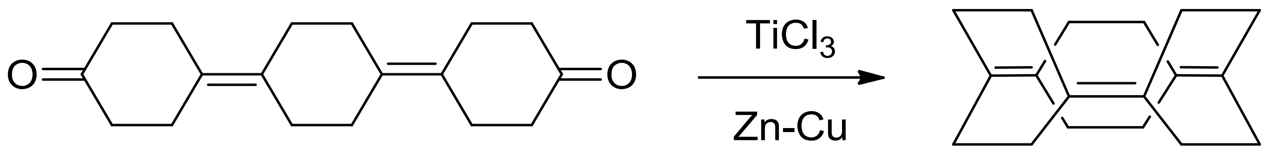


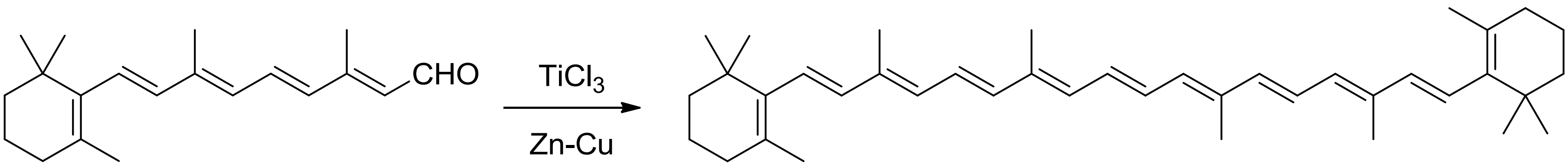


25%

Review:
A. Fürstner, Ed. M. Beller, C. Bolm, Transition Metals for Organic Synthesis (2nd Edition) **2004**, *1*, 449.

Titanium

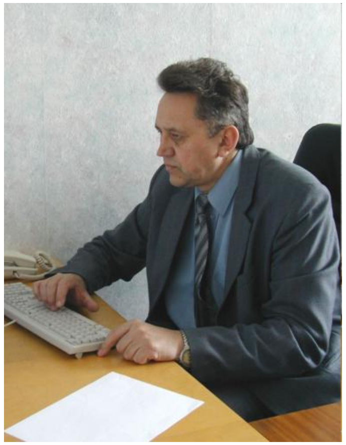




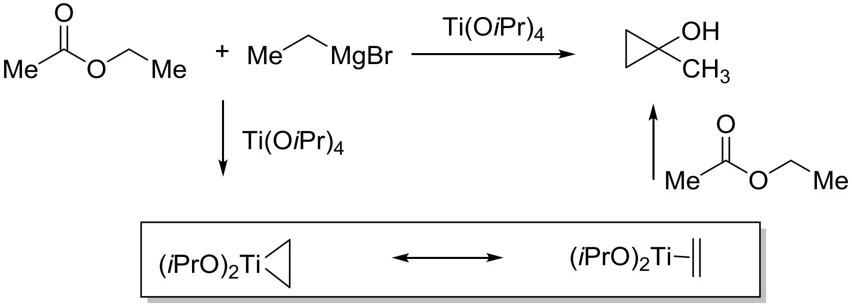
β -Caroten: 94%

J. E. McMurry et al. *J. Am. Chem. Soc*. **1984**, *106*, 5018.

Titanium

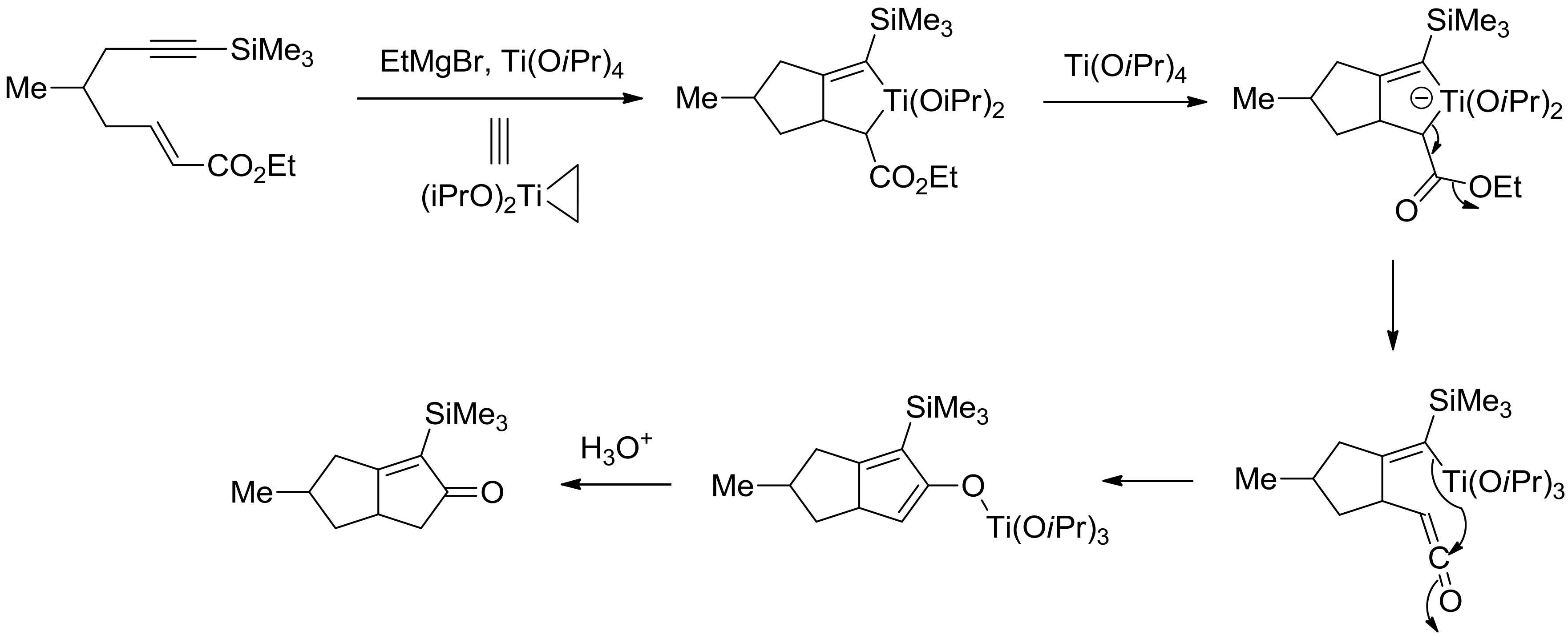


Kulinkovich-reaction



O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, T. S. Pritytskaya, *Zh. Org. Khim.* **1989**, 25, 2244.
O. Kulinkovich, S.V. Sviridov, D.A. Vasilevski, *Synthesis, **1991***, 234.

Titanium



F. Sato *J. Org. Chem*. **1988**, *53*, 5590.

Early transition metal organometallics: Zirconium

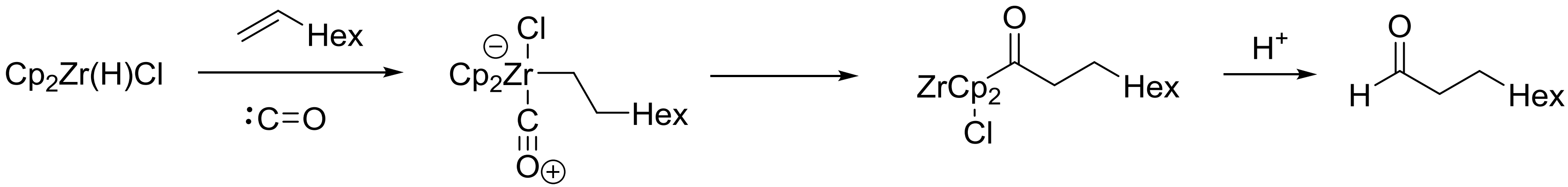
Schwartz's reagent:

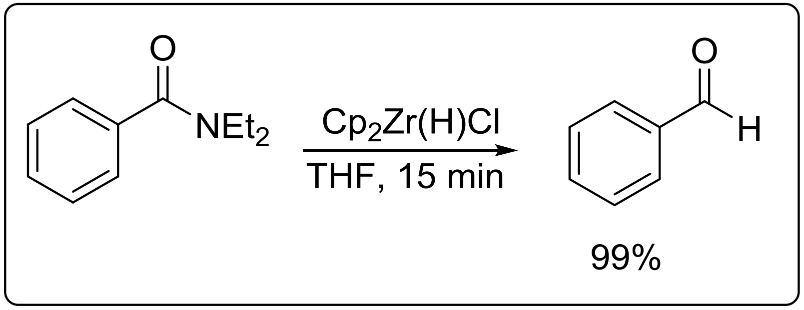
$$ZrCp_2Cl_2 \xrightarrow[\text{THF}]{\text{LiAl(H)(O}t\text{Bu)}_3} Cp_2Zr(H)Cl$$

90%

Inorg. Synth. **1979**, *19*, 223

Zirconium

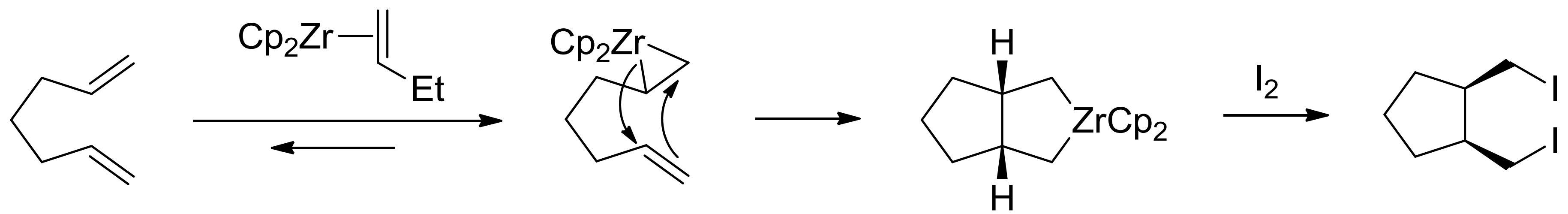


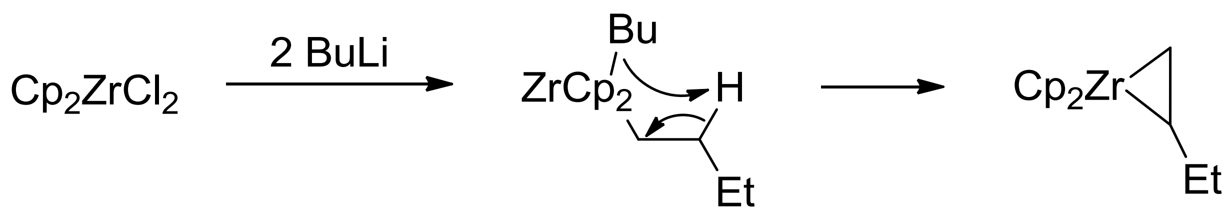


G. I. Georg *J. Am. Chem. Soc*. **2007**, *129*, 3408

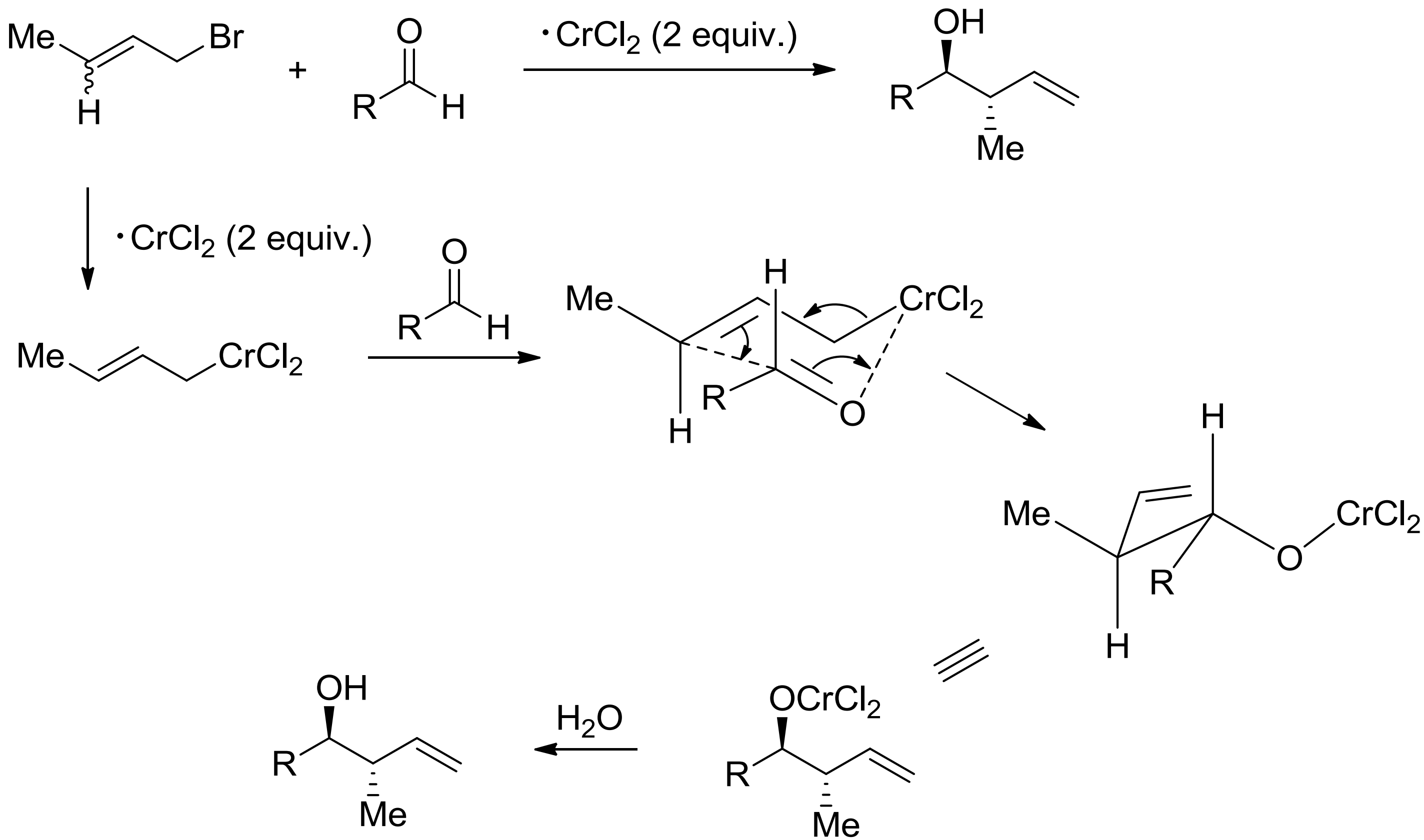
Zirconium

A Negishi reaction is involved:



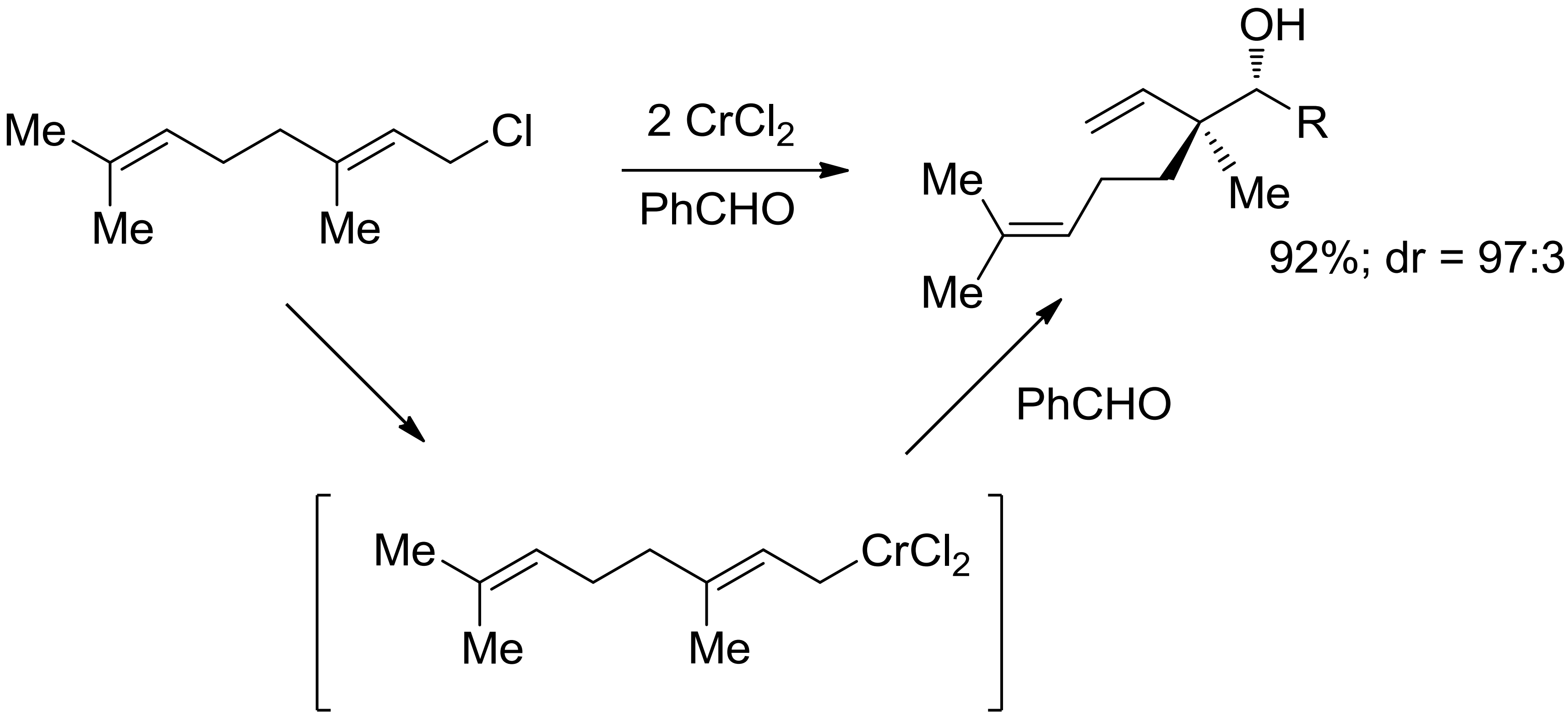


Early transition metal organometallics: Chromium



Hiyama reaction *Bull. Soc. Chem. Jpn* **1982**, *55*, 567; *J. Am. Chem. Soc*. **1977**, *99*, 3175

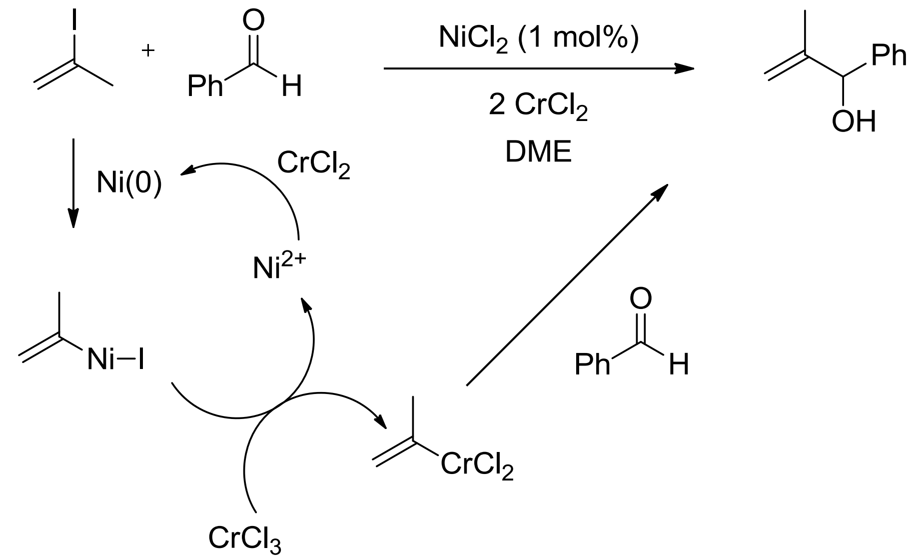
Chromium

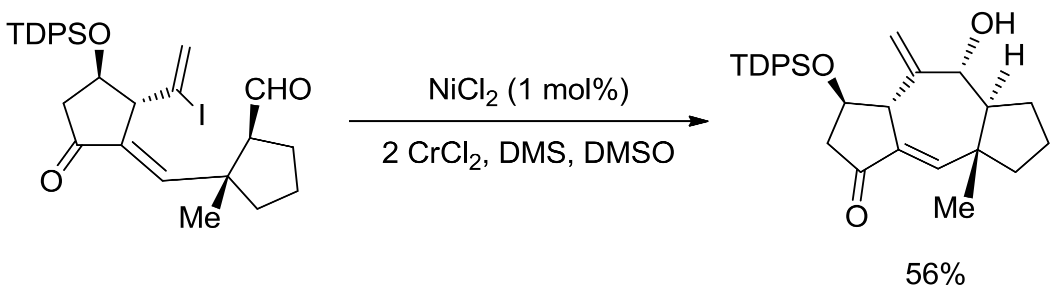


K. Belyk, M. J. Rozema, P. Knochel *J. Org. Chem*. **1992**, *57*, 4070.

Chromium

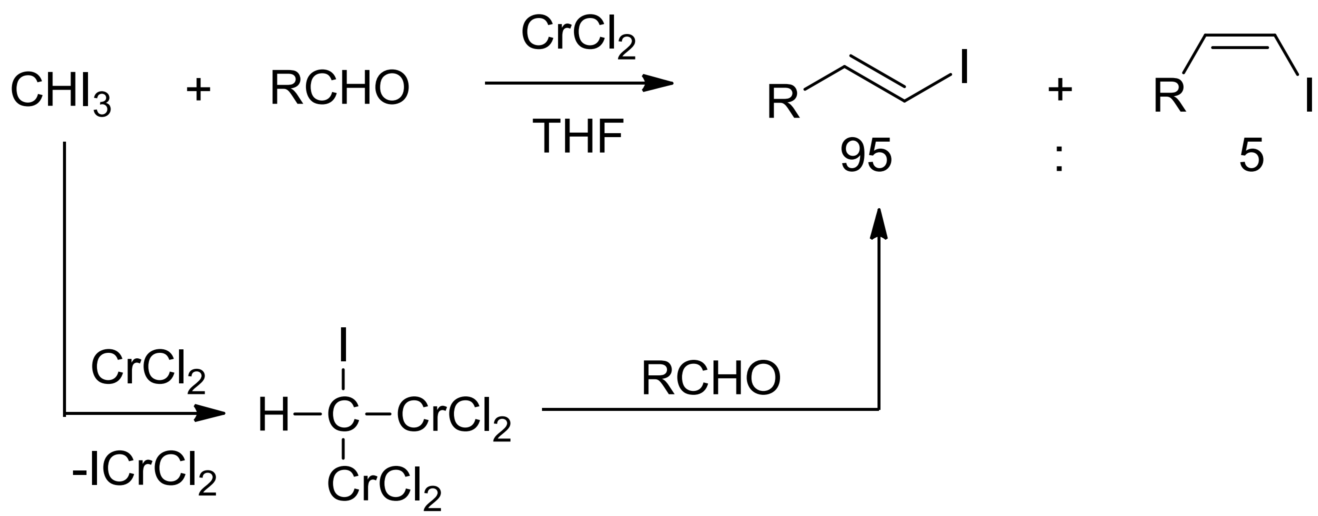
Hiyama-Kishi-reaction

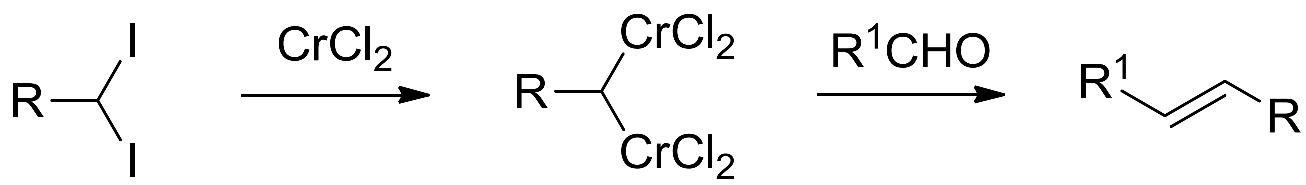




Y. Kishi *J. Am. Chem. Soc*. **1989**, *111*, 2735.

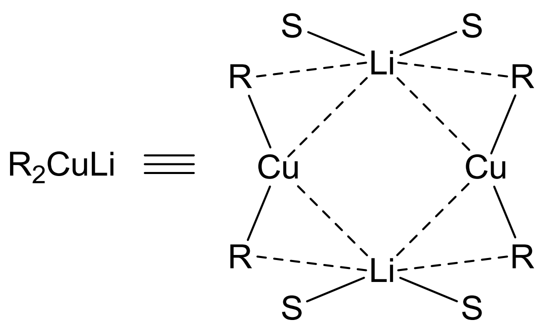
Chromium

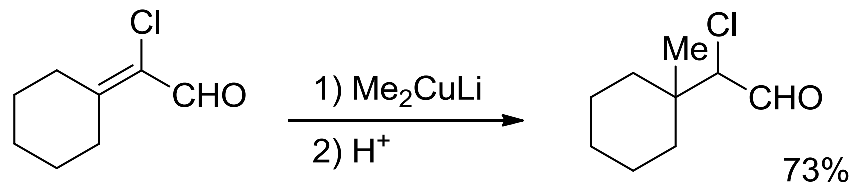


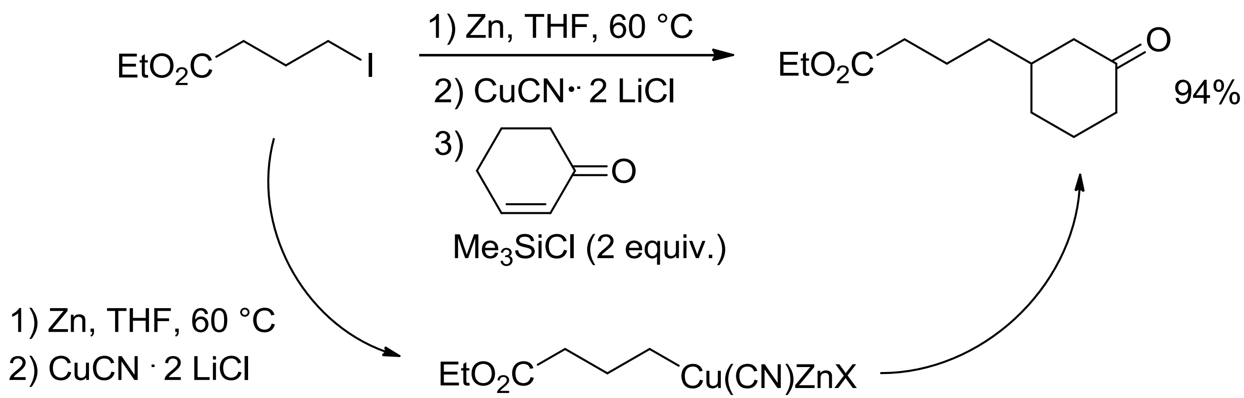


K. Takai *J. Am. Chem. Soc*. **1986**, *108*, 7408

Early transition metal organometallics: **Copper**

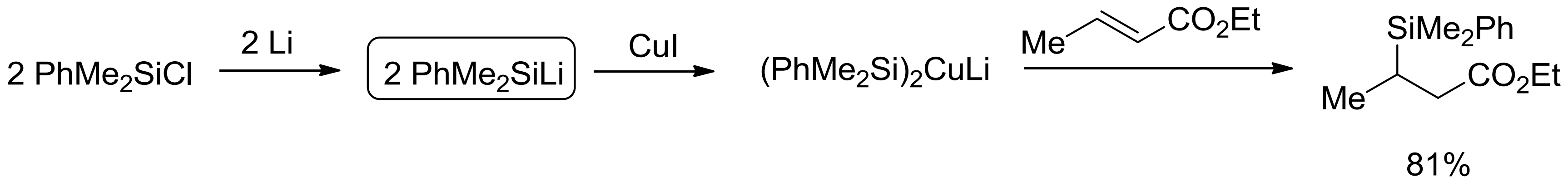




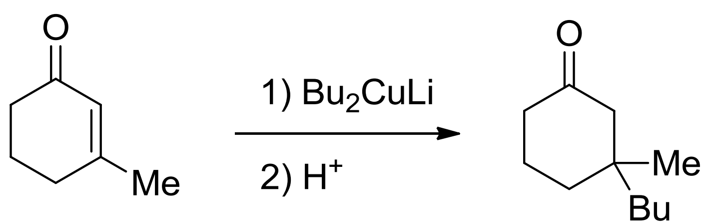


P. Knochel, et al. *J. Org. Chem*. **1988**, *53*, 2390.

Copper



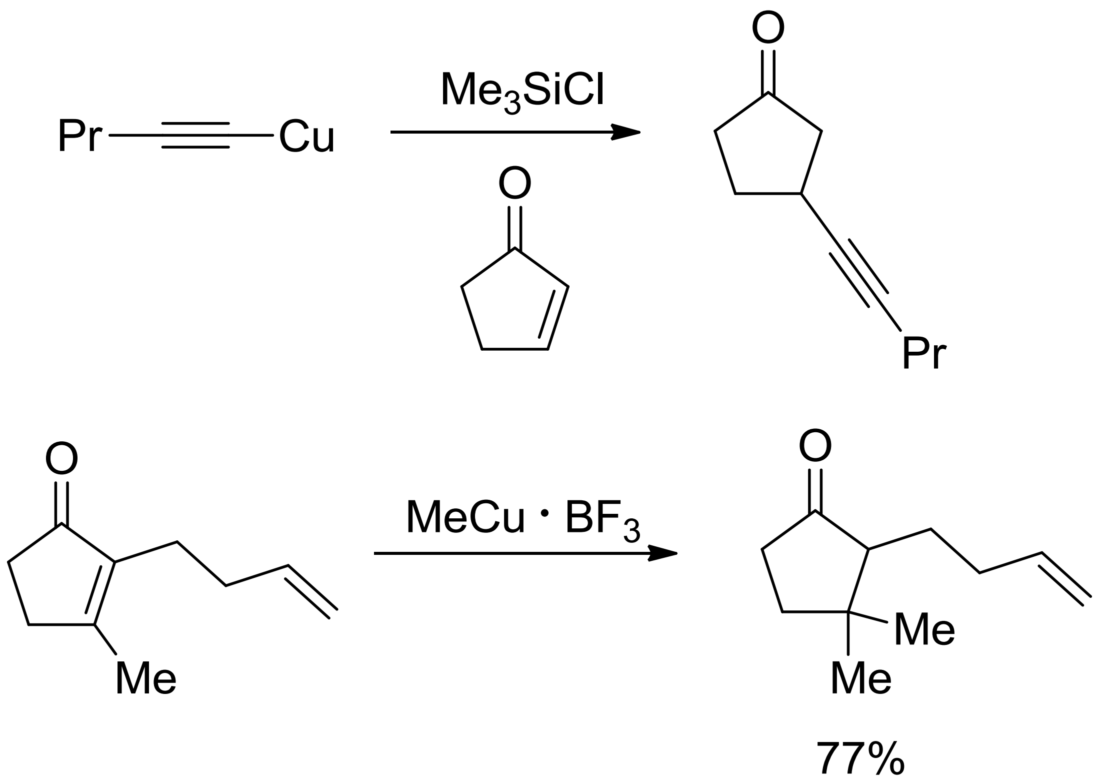
I. Fleming et al. *J. Chem. Soc., Perkin Trans*. **1998**, *1*, 1209.



without additives: 28%
Me_3SiCl (2 equiv.): 99%

E. Nakamura et al. *Tetrahedron Lett*. **1986**, *27*, 4029.

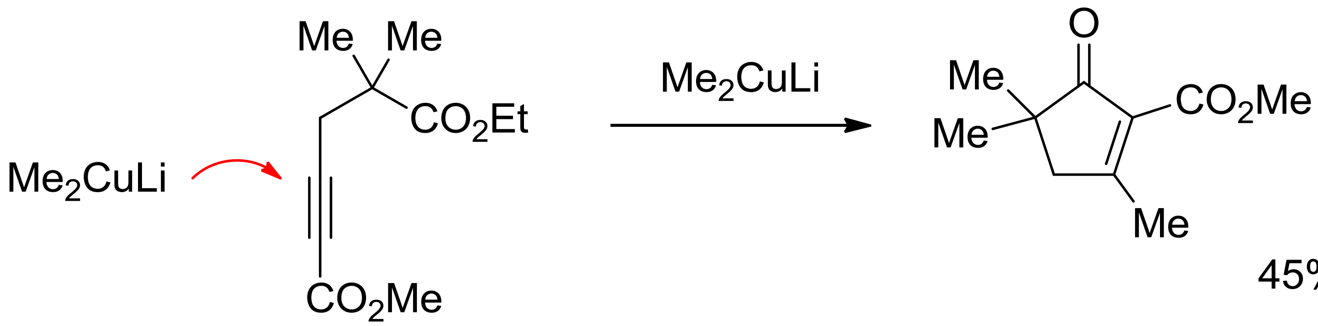
Copper-mediated 1,4-addition



Y. Yamamoto, *Angew. Chem*. **1986**, *98*, 945.

Copper-mediated reactions

Michael-addition



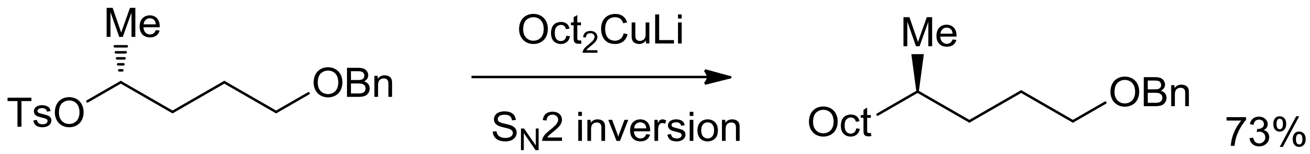
45%

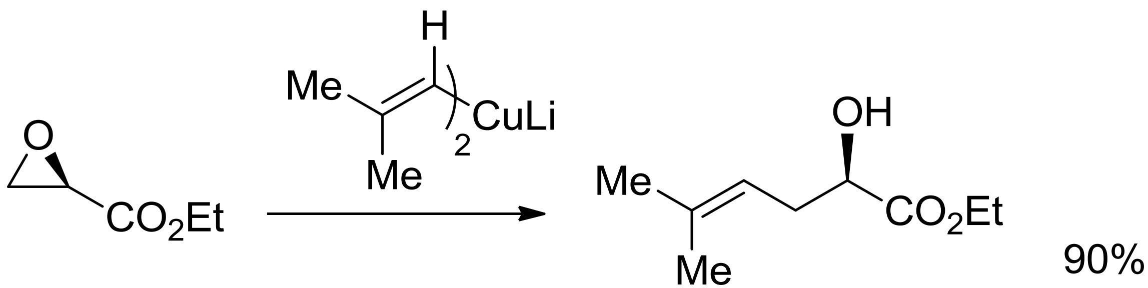
Substitution reactions

80%

G. Posner, *Org. React*. **1975**, *22*, 253.
R. J. K. Taylor (Ed.), *Organocopper reagents*, Oxford University Press, Oxford, **1994**.

Copper; substitution reactions

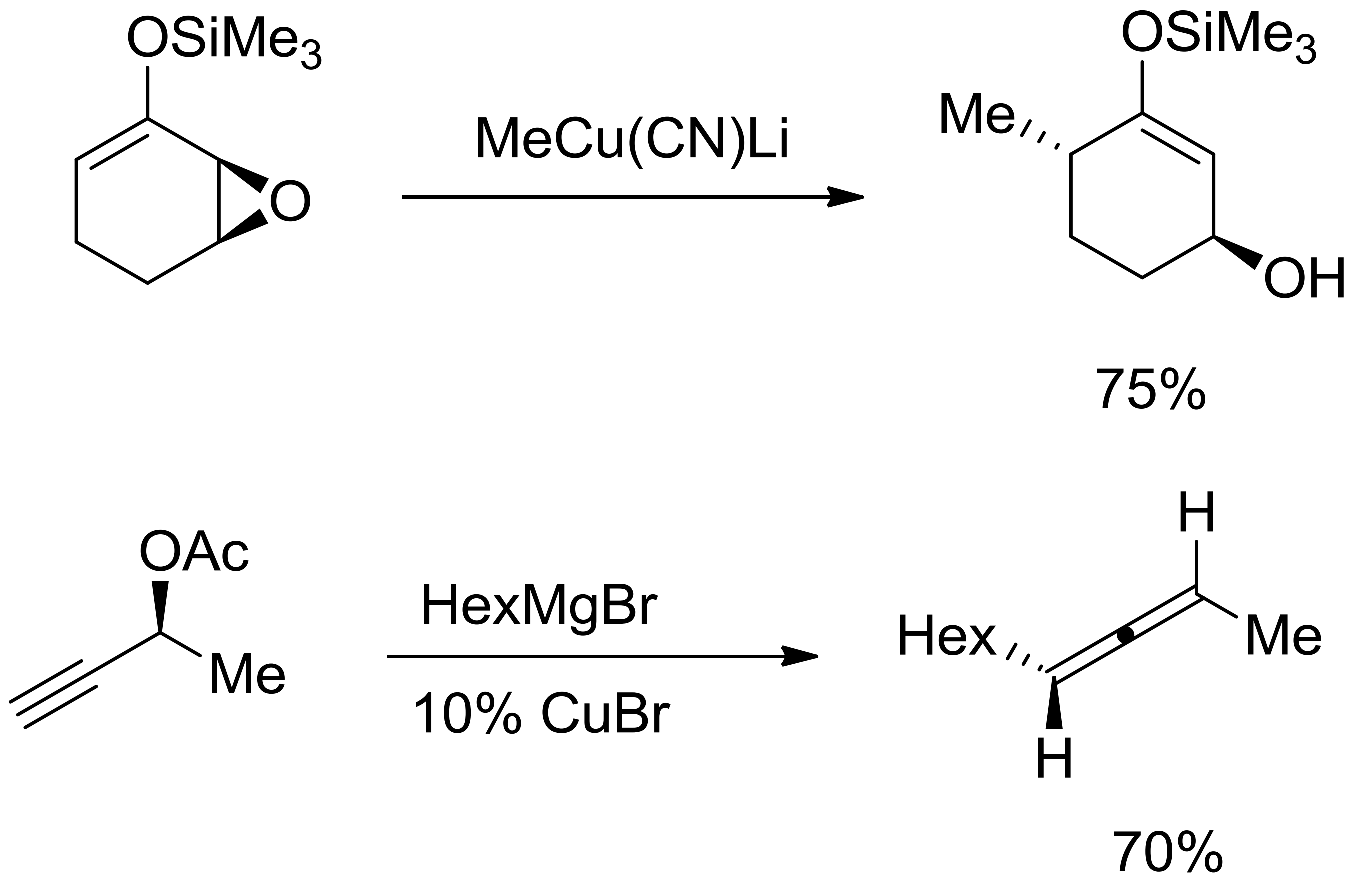




*t*BuMgCl + $PhCH_2Cl$ $\xrightarrow[\text{0.25 mol\%}]{Li_2CuCl_4}$ $PhCH_2$*t*Bu

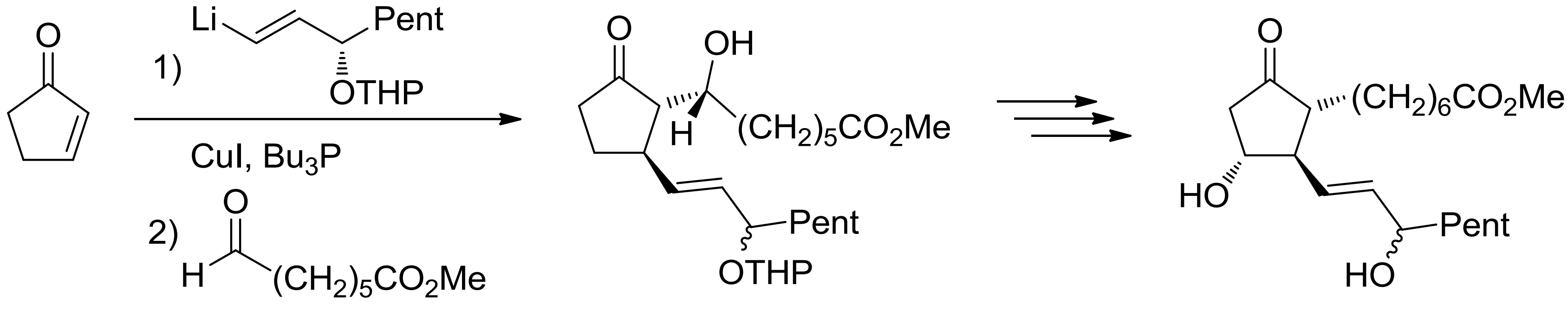
M. Larcheveque, Y. Petit, *Bull. Soc. Chim. Fr*. **1989**, *1*, 130.

Copper: allylic and propargylic substitution



A. Alexakis, *Pure Appl. Chem.* **1992**, *64*, 387.

Copper: Prostaglandin synthesis



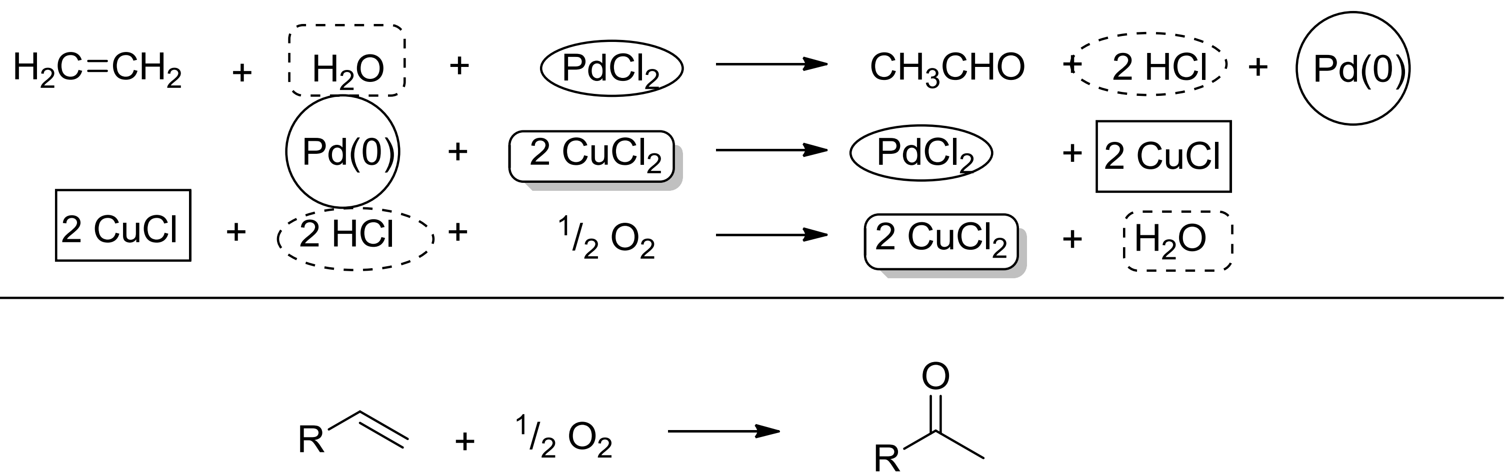
Prostaglandin E1

F. Sato *J. Org. Chem*. **1988**, *53*, 5590

Palladium

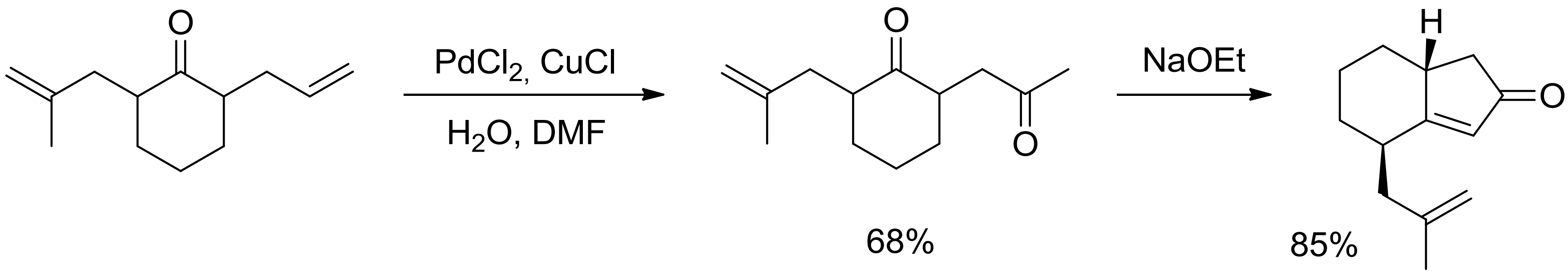
Price of Pd: **1.0**
Pt: 3.3
Au: 1.9
Ru: 0.2
Rh: 2.8

Wacker-Reaction:



J. Schmidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier, J. Sabel, *Angew. Chem. Int. Ed*. **1962**, *1*, 80.

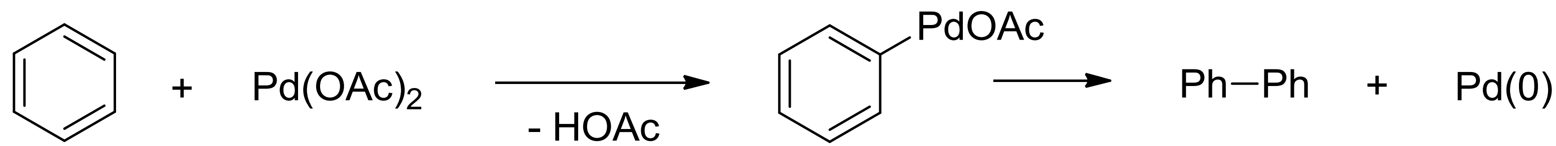
Palladium

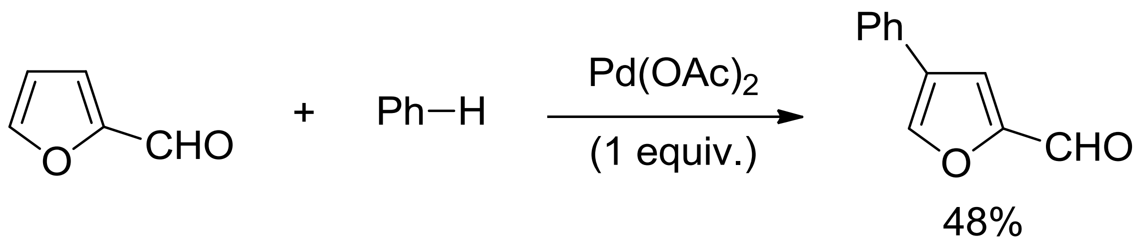


J. Tsuji, I. Shimizu, K. Yamamoto, *Tetrahedron Lett*. **1976**, *34*, 2975.

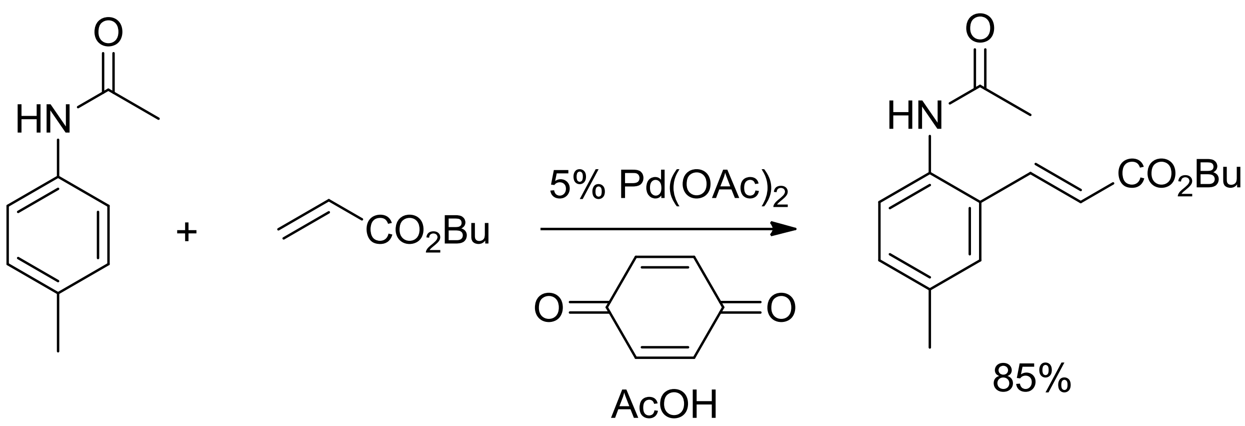
Palladium

C-H activation



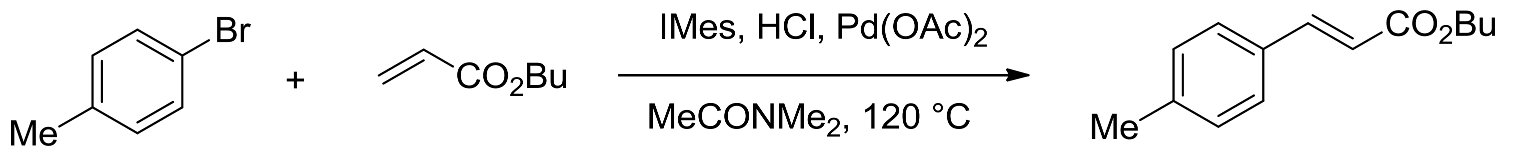


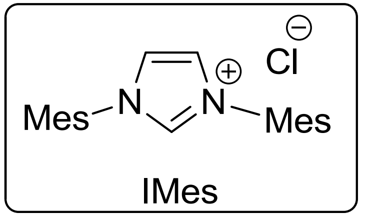
T. Itahara, *J. Org. Chem*. **1985**, *50*, 5272.



J. G. de Vries *J. Am. Chem. Soc*. **2002**, *124*, 1586.

Heck Reaction





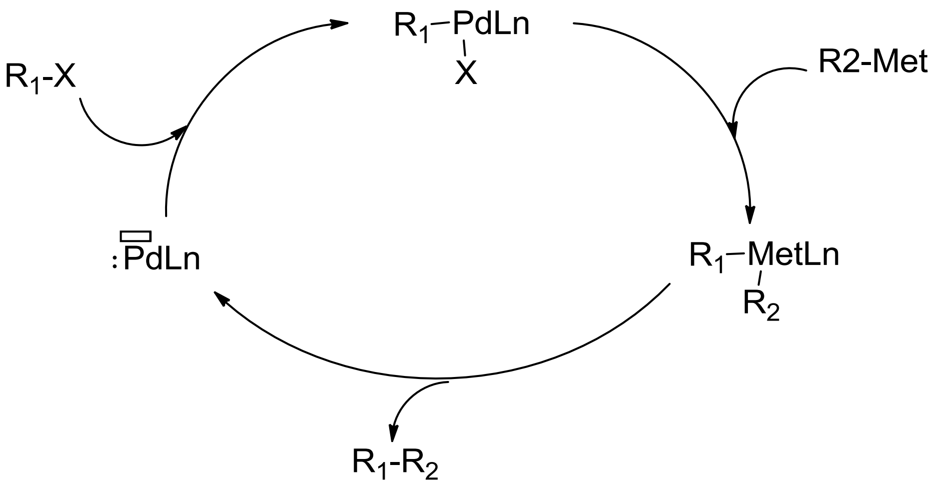
The method of T. Jeffery uses Bu_4NBr at 25 °C.

T. Jeffery *Chem. Comm*. **1984**, 1287

Palladium-catalyzed cross-coupling

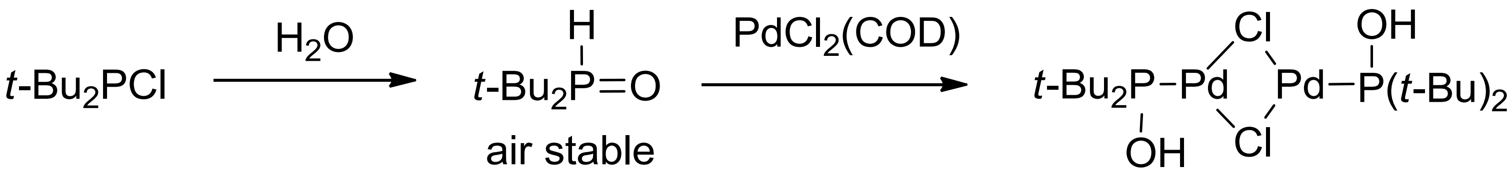
Cross-coupling using Pd(0)-catalysts

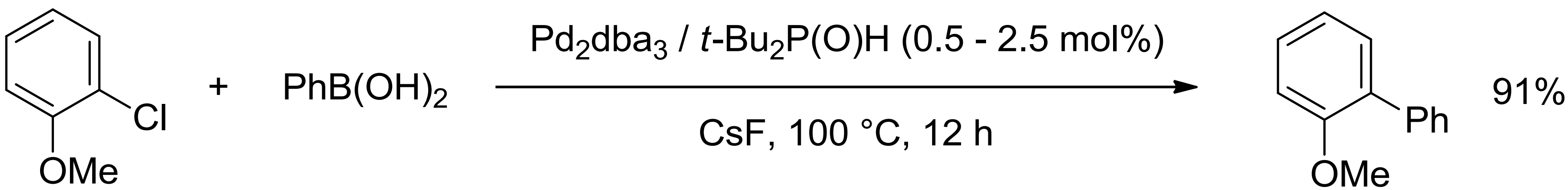
$$R_1\text{-}X \quad + \quad R_2\text{-Met} \xrightarrow[\text{Pd(0) or Ni(0)}]{} R_1\text{-}R_2$$



Suzuki-coupling	Met = $B(OH)_2$
Stille-coupling	Met = SnR_3
Negishi-coupling	Met = ZnX
Kumada-coupling	cat = Ni; Met = MgX
Sonogashira-coupling	Csp-Csp^2

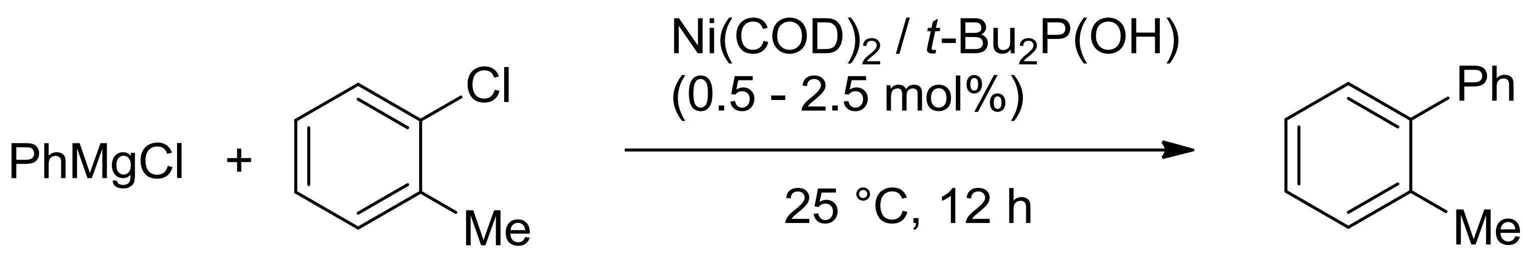
Palladium

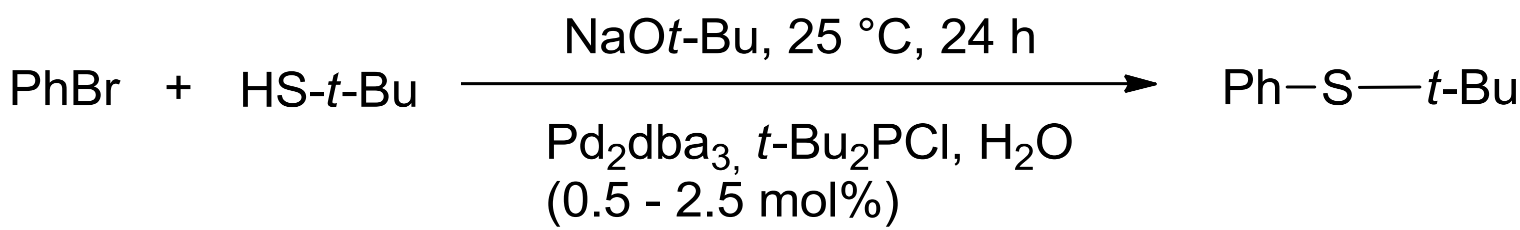




G. Y. Li, *Angew. Chem. Int. Ed*. **2001**, *40*, 1513.

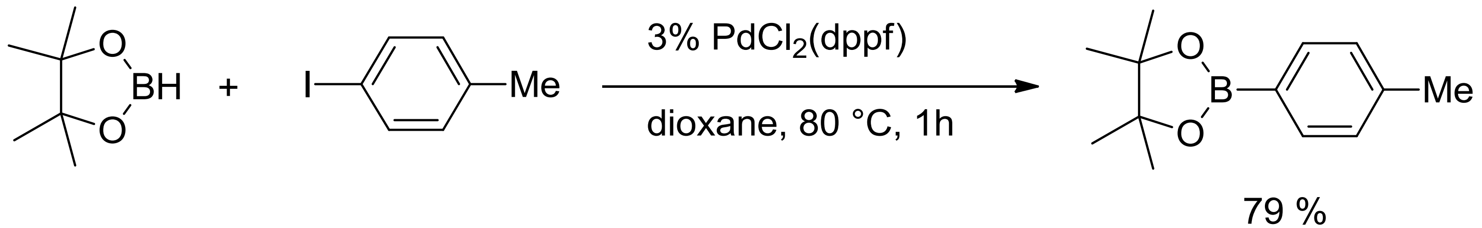
Palladium



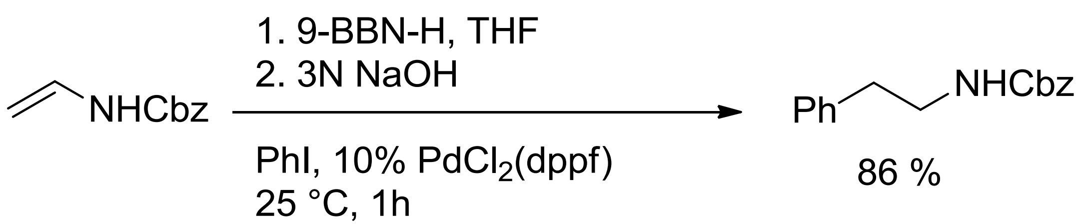


G. Y. Li, *Angew. Chem. Int. Ed*. **2001**, *40*, 1513.

Palladium

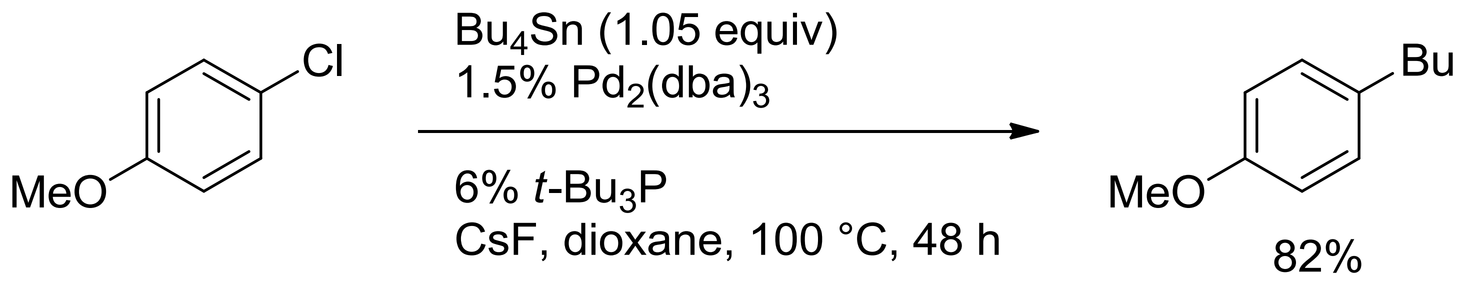


M. Murata, *J. Org. Chem*. **2000**, *65*, 164.



L. E. Overman, *J. Org. Chem*. **1999**, *64*, 8743.

Stille cross-coupling



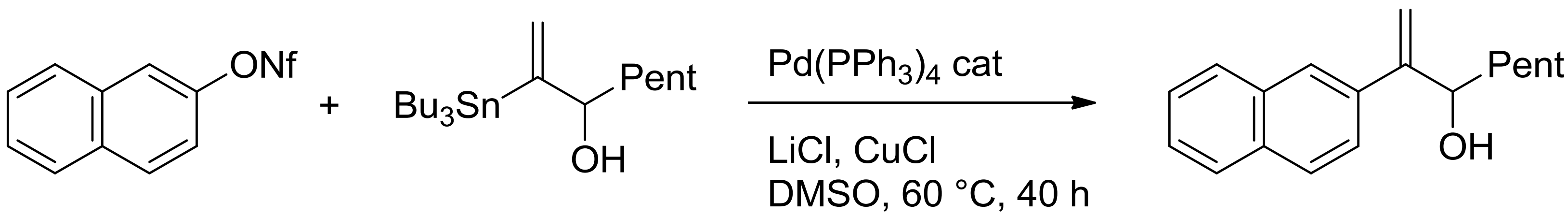
G. C. Fu, *Angew. Chem. Int. Ed*. **1999**, *38*, 2411.

On the mechanism of the Stille cross-coupling:

P. Espinet *J. Am. Chem. Soc*. **1998**, *120*, 8978.
J. Am. Chem. Soc. **2000**, *122*, 1771.

Palladium

Cu-accelerated Stille-reaction

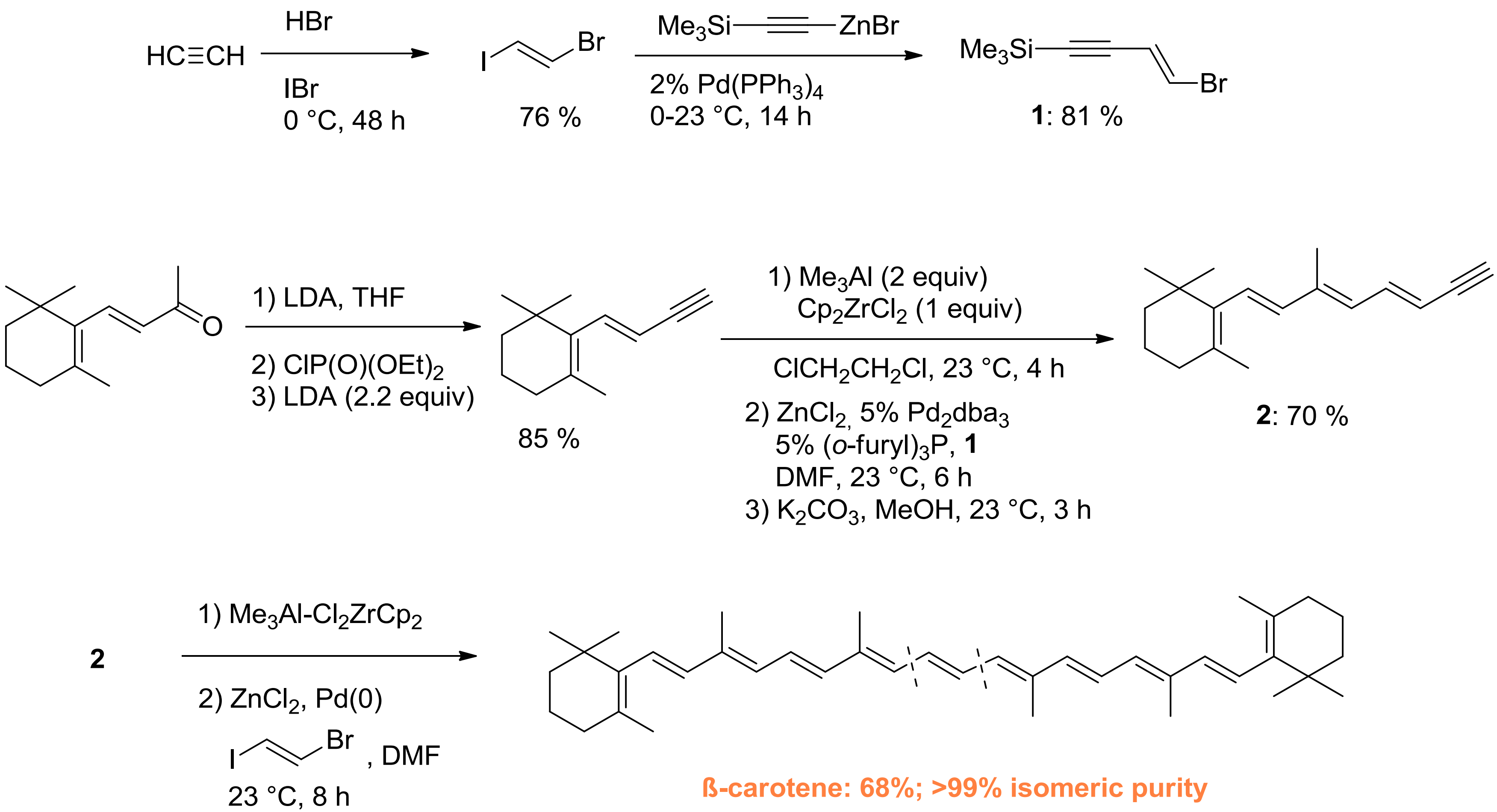


88%

E. J. Corey, *J. Am Chem. Soc*. **1999**, *121*, 7600.

Negishi reactions

Synthesis of carotenoids *via* Zr-catalyzed carboalumination and Pd /Zn-catalyzed cross-couplings:

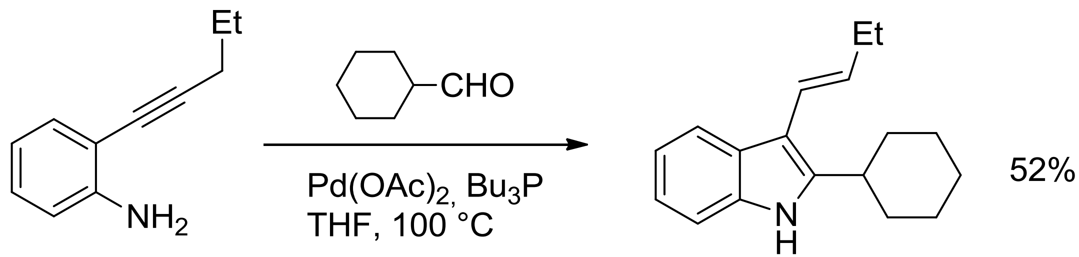


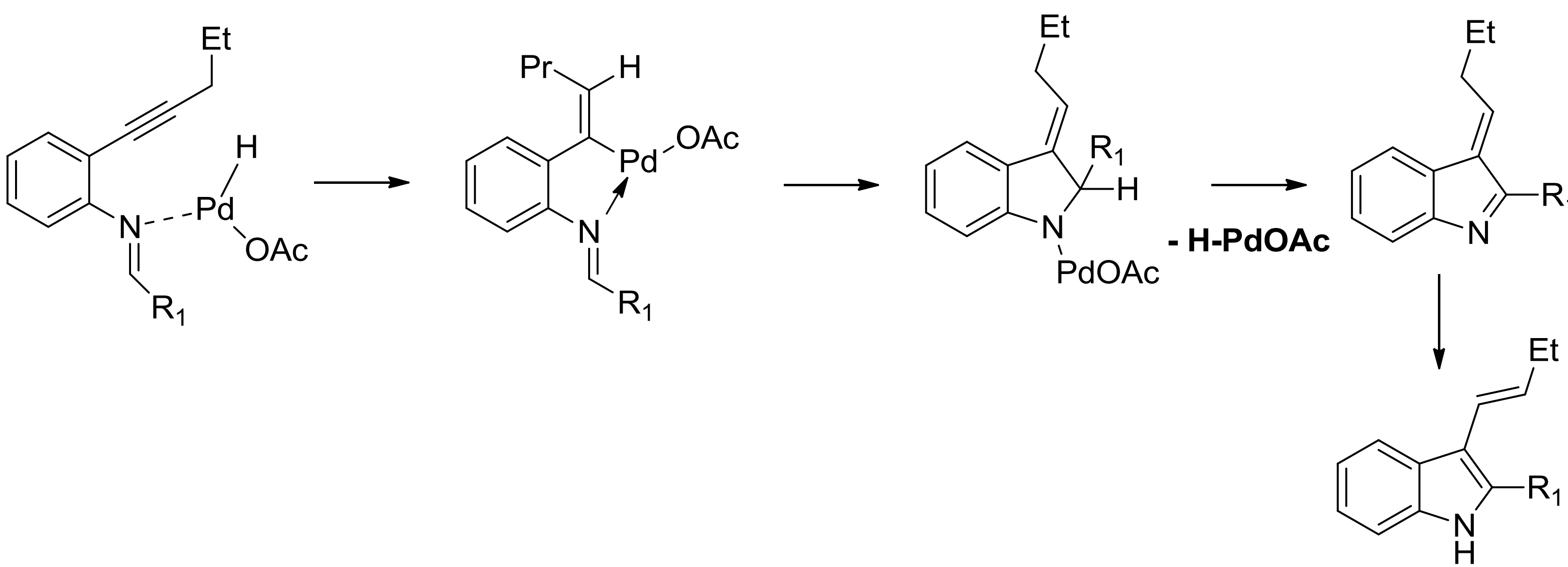
ß-carotene: 68%; >99% isomeric purity

E. Negishi, *Org. Lett*. **2001**, *3*, 719.

Palladium

Example of an indole synthesis *via* an intramolecular cyclization of alkynes and imines using a Pd-catalyst:

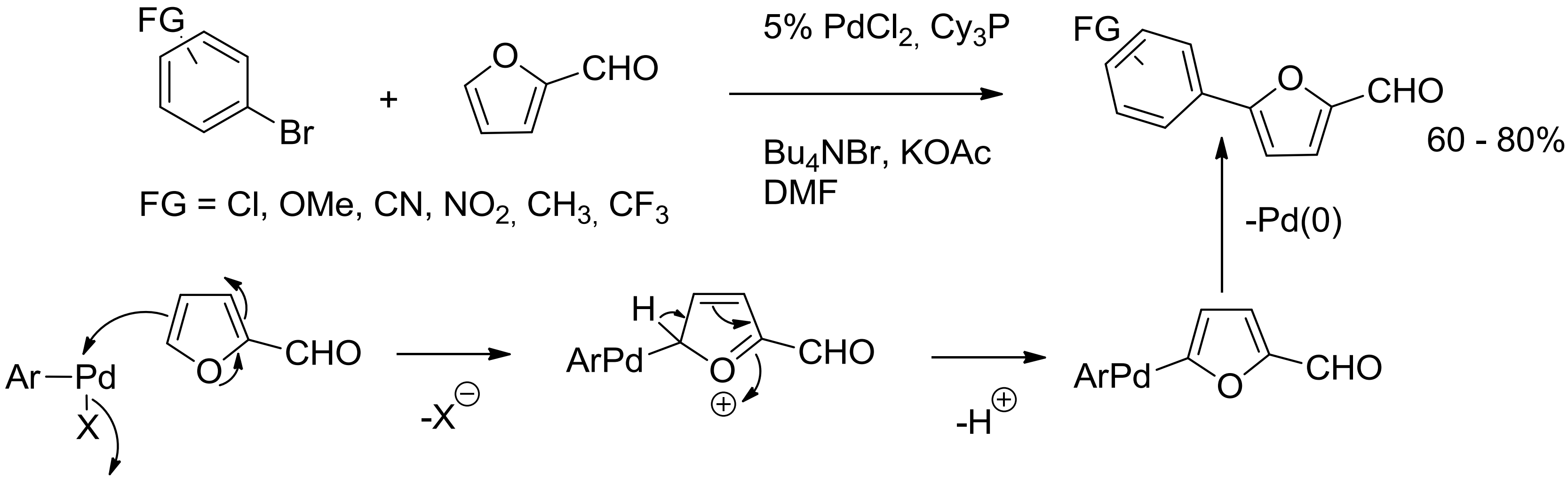




H. Yamamoto, *J. Am. Chem. Soc*. **2000**, *122*, 5662.

Palladium

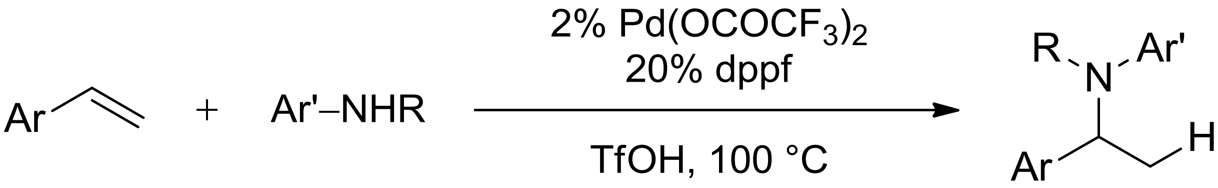
Regioselective Pd-catalyzed arylation of 2-furaldehyde using a C-H activation

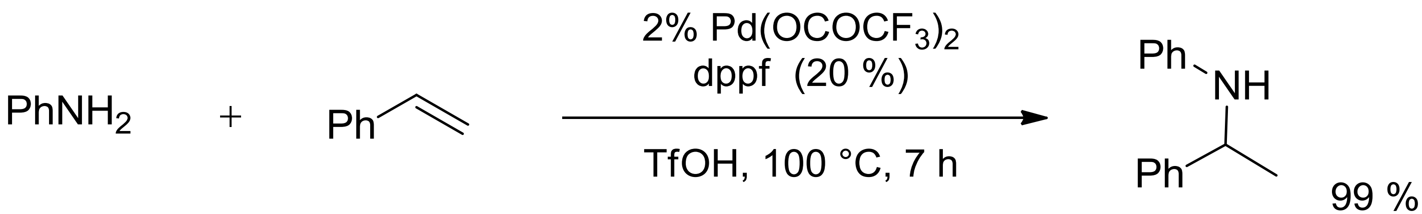


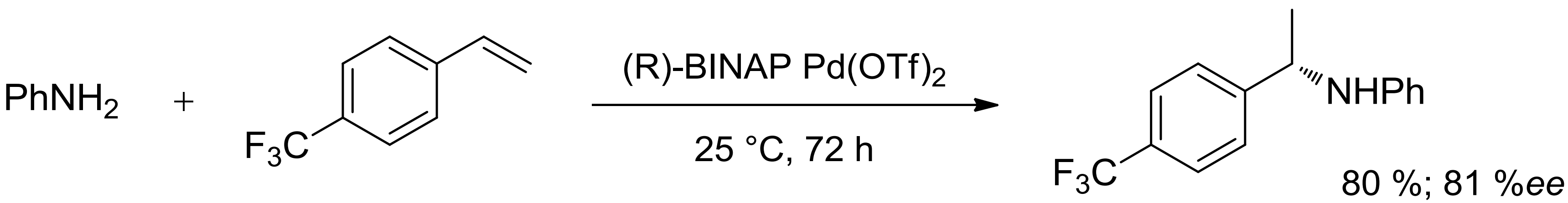
M. S. McClure, *Org. Lett*. **2001**, *3*, 1677

Palladium

Pd - catalyzed hydroamination of vinylarenes

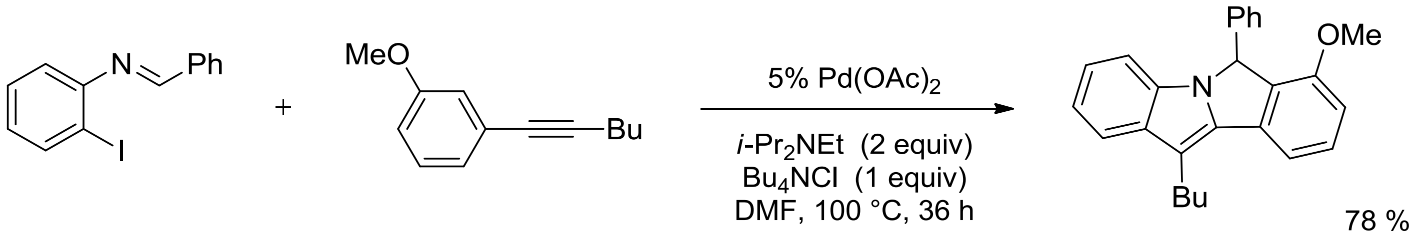




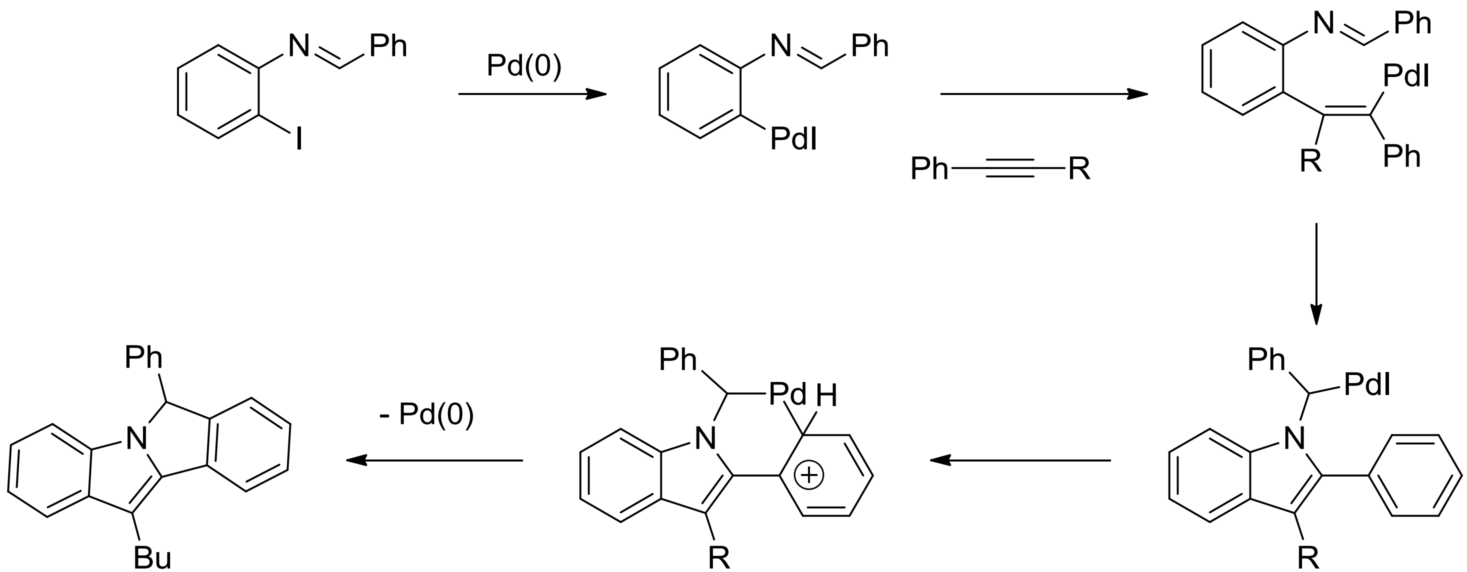


H. Hartwig *J. Am. Chem. Soc*. **2000**, *122*, 9546

Pd -catalyzed heterocycle synthesis

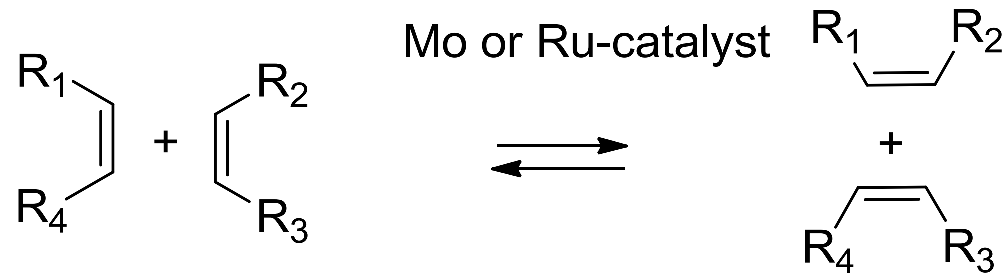


Mechanism



R.C. Larock, *J. Org. Chem*. **2001**, *66*, 412

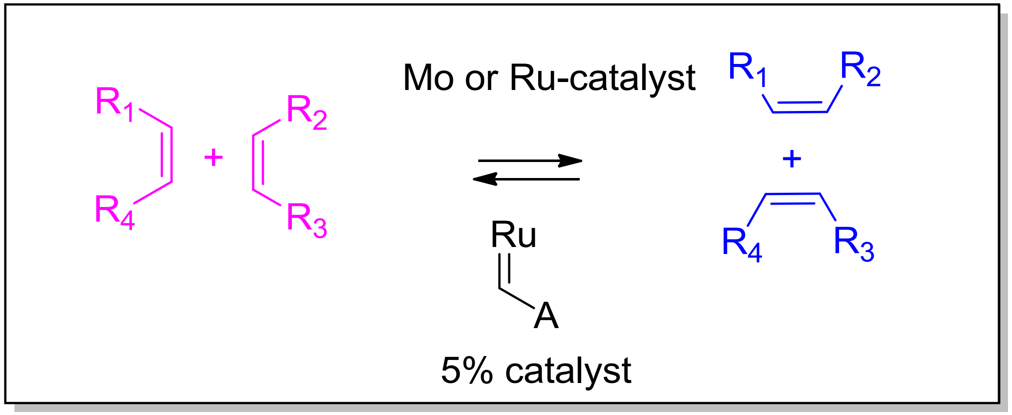
Olefin metathesis

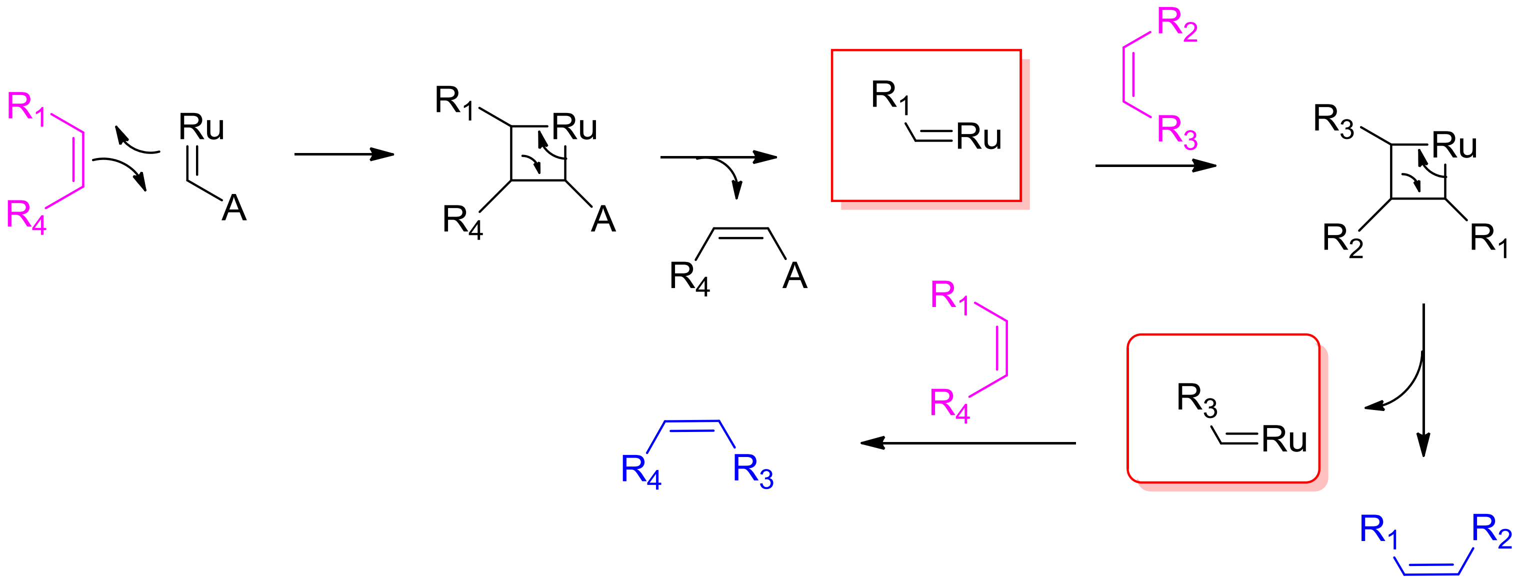


Reviews:

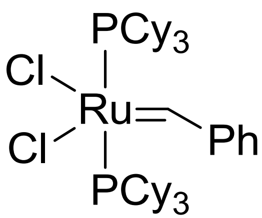
R.H. Grubbs, *Tetrahedron* **1998**, *54*, 4413.
A.S.K. Hashmi, *J. Prakt. Chemie* **1997**, *339*, 1954.
M.E. Maier, *Angew. Chem. Int. Ed*. **2000**, *39*, 2073.
S.Blechert, *Angew. Chem*. **1997**, *109*, 2124.
A.Fürstner, (Ed.) Alkene Metathesis in Organic Synthesis
in Top. Curr. Chem., Springer Verlag, Berlin, **1998**.
E.M. Carreira, *Synthesis* **2000**, 857.
Mechanistic study: R.H. Grubbs, *J. Am. Chem. Soc*. **2001**, *123*, 749.

Olefin metathesis mechanism

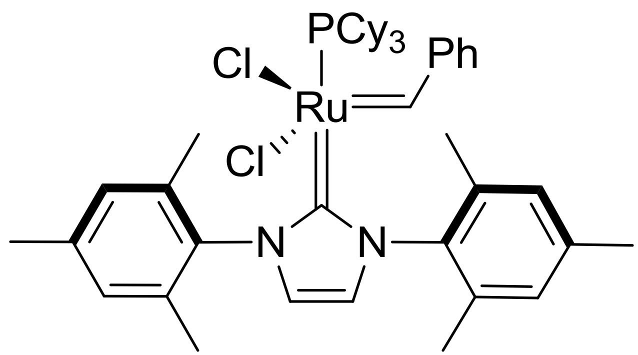




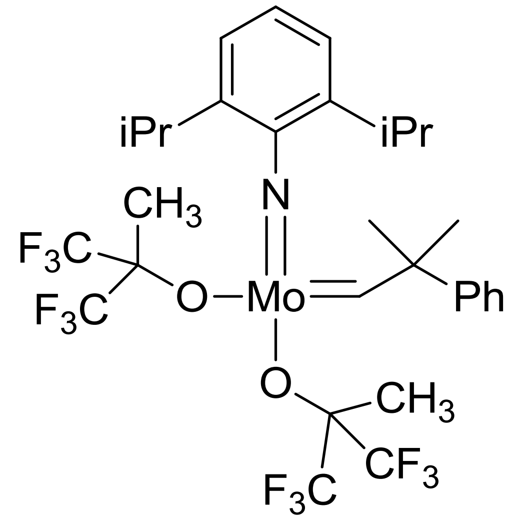
Olefin metathesis



1: Grubbs-catalyst
first generation
J. Am. Chem. Soc.
1995, *117*, 2108.

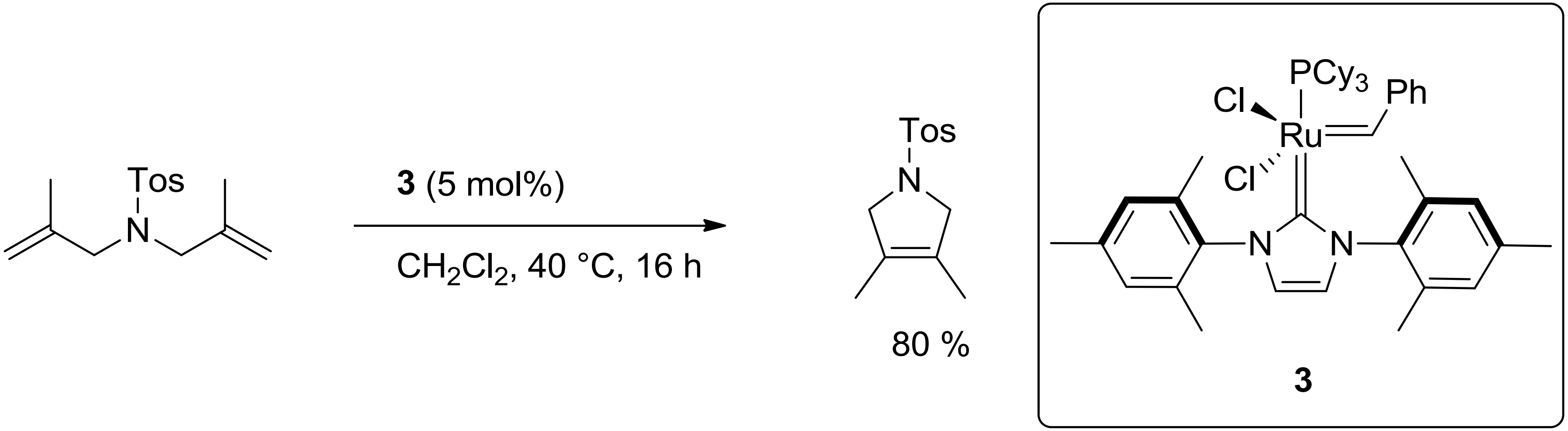


2: Grubbs-catalyst
second generation
US Patent No. 6,111,121
and 7,329,758



3: Schrock-catalyst
J. Am. Chem. Soc.
1998, *120*, 4041.

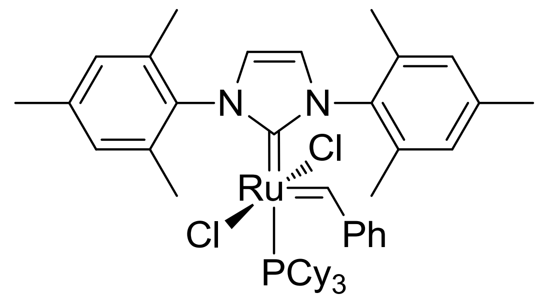
Olefin metathesis



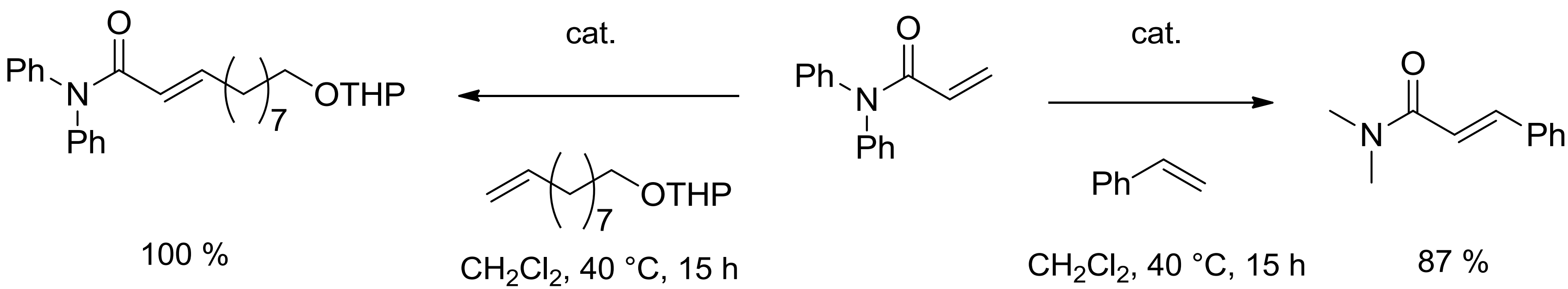
A. Fürstner, W.A. Herrmann, *Tetrahedron Lett*. **1999**, *40*, 4787

Olefin metathesis

Synthesis of α,β -unsaturated amides by olefin cross-metathesis



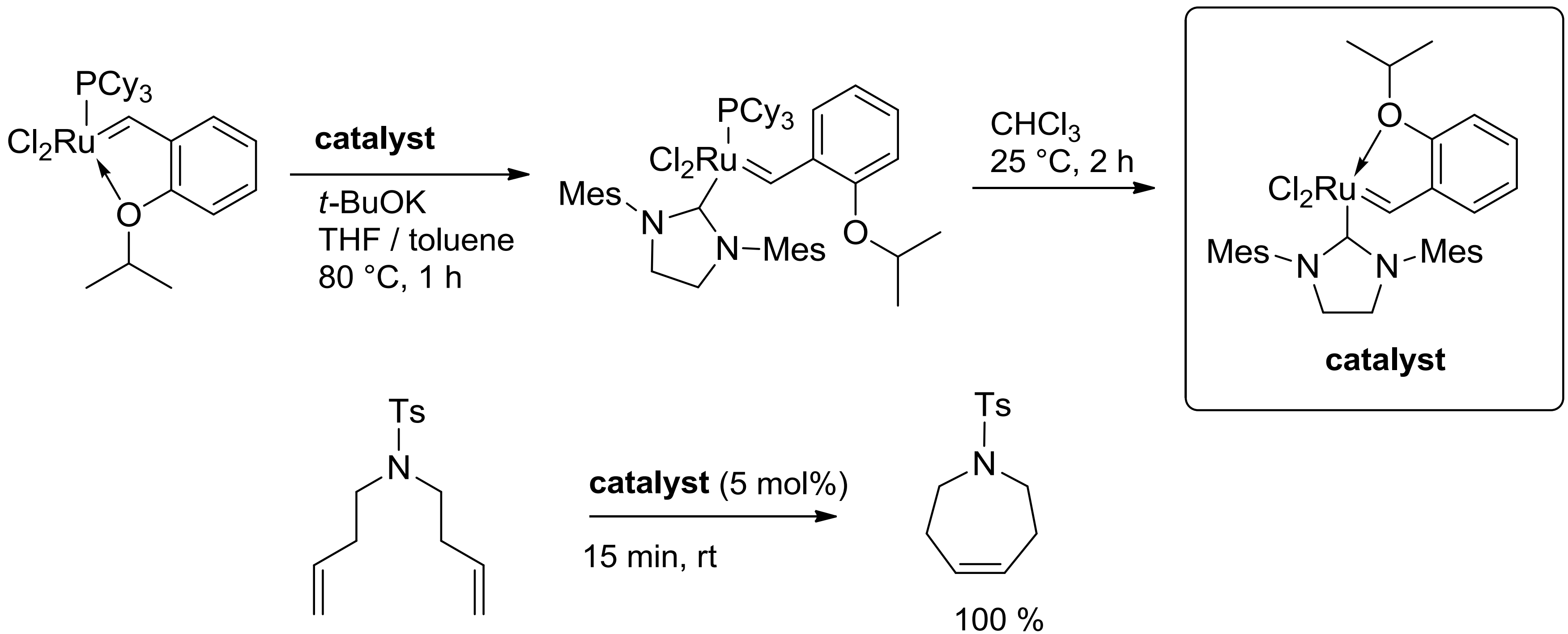
Cat.



R. H. Grubbs, *Angew. Chem. Int. Ed*. **2001**, *40*, 1277

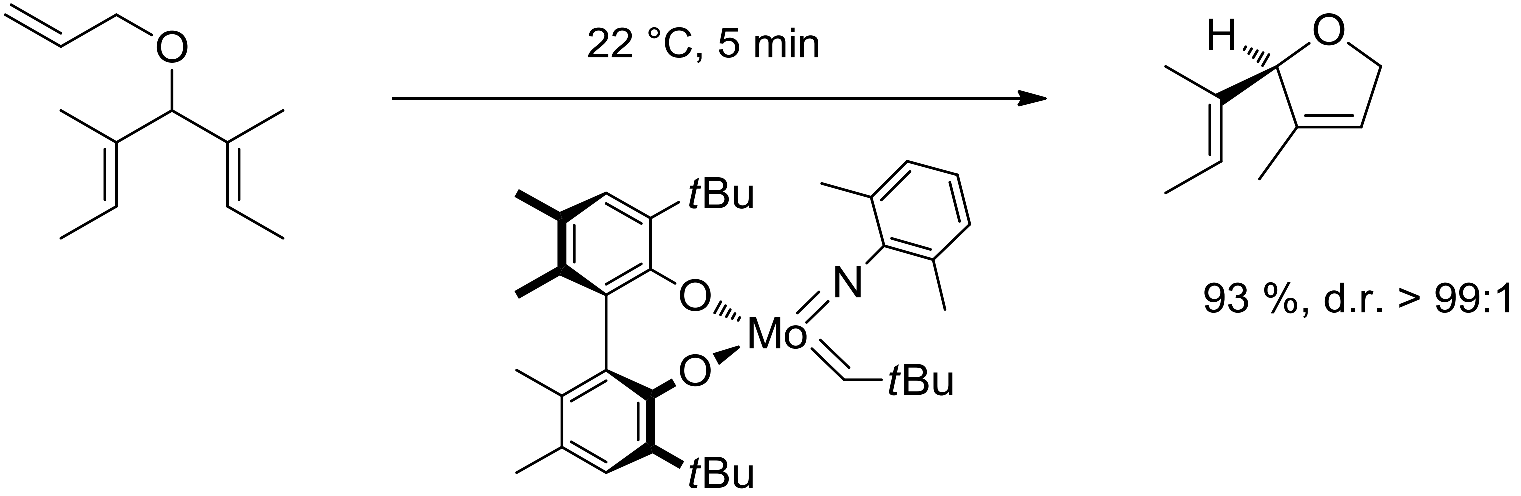
Olefin metathesis

New phosphine-free metathesis catalyst



S. Blechert, *Tetrahedron Lett*. **2000**, *41*, 9973

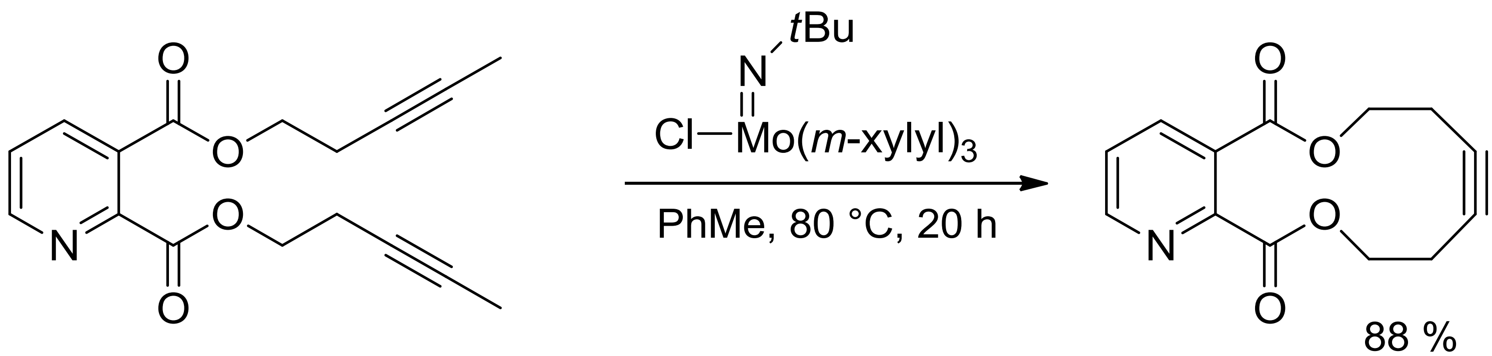
Enantioselective metathesis reaction



A.H. Hoveyda, R.R. Schrock, *J. Am. Chem. Soc*. **1998**, *120*, 9720
J. Am. Chem. Soc. **1999**, *121*, 8251
J. Am. Chem. Soc. **2001**, *123*, 7767

Olefin metathesis

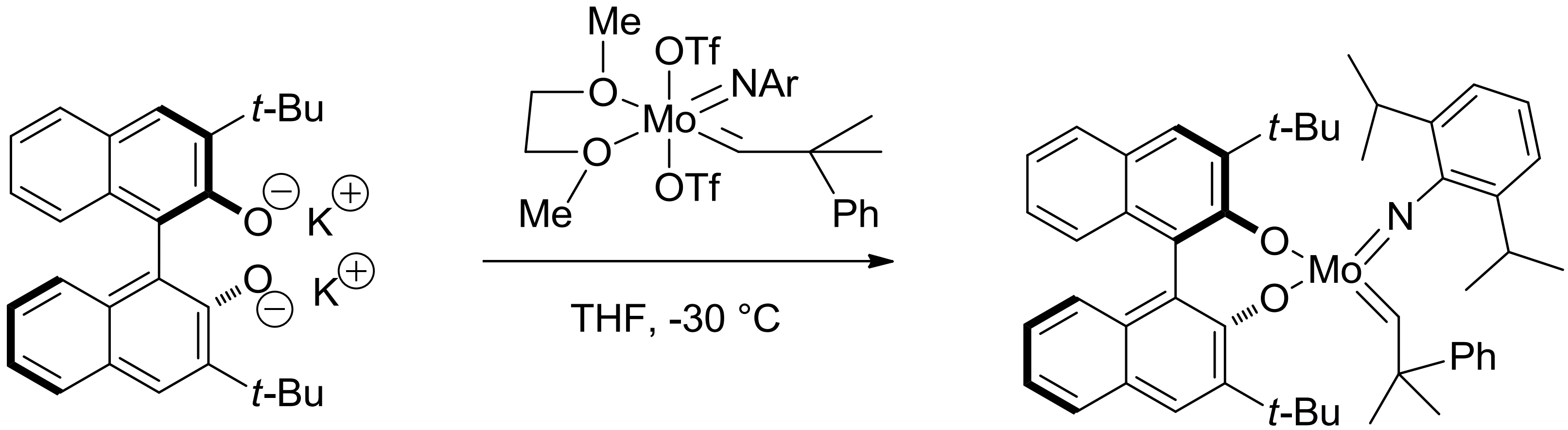
Metathesis of alkynes



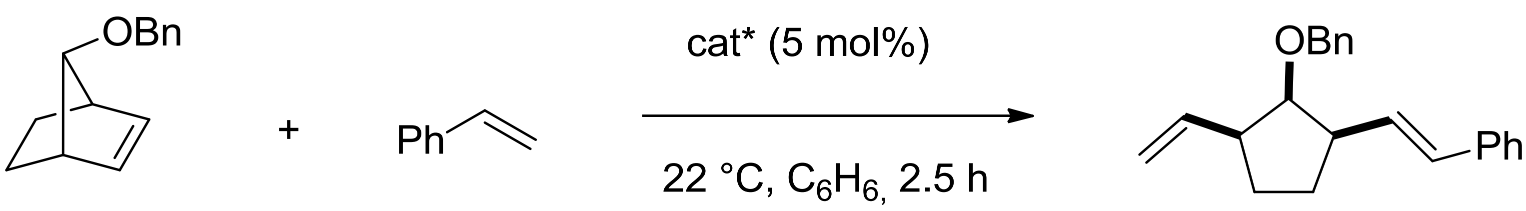
A. Fürstner, *J. Am. Chem. Soc*. **1999**, *121*, 9453.
J. Heppekausen, A. Fuerstner, *Angew. Chem. Int. Ed*. **2011**, *50*, 7829.

Olefin metathesis

User-friendly chiral catalyst for enantioselective olefin metathesis



cat*

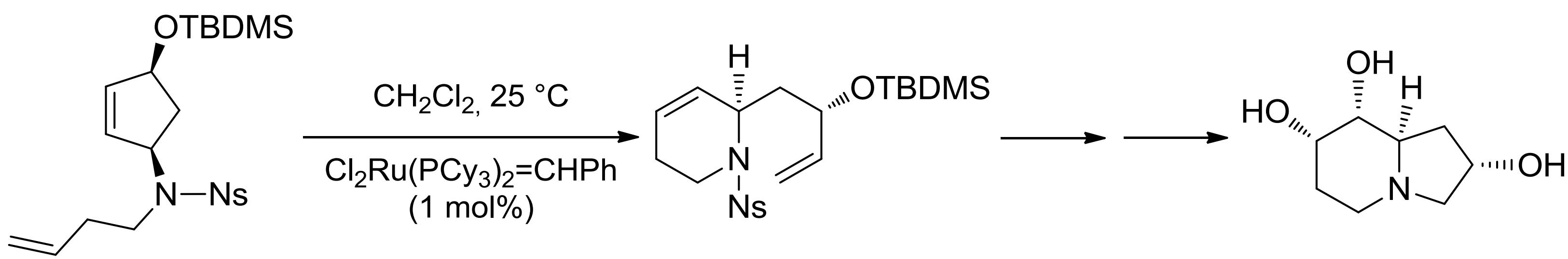


86%; >98% ee

A. H. Hoveyda, R. R. Schrock, *Angew. Chem. Int. Ed*. **2001**, *40*, 1452

Application to the synthesis of natural products

Synthesis of aza sugars

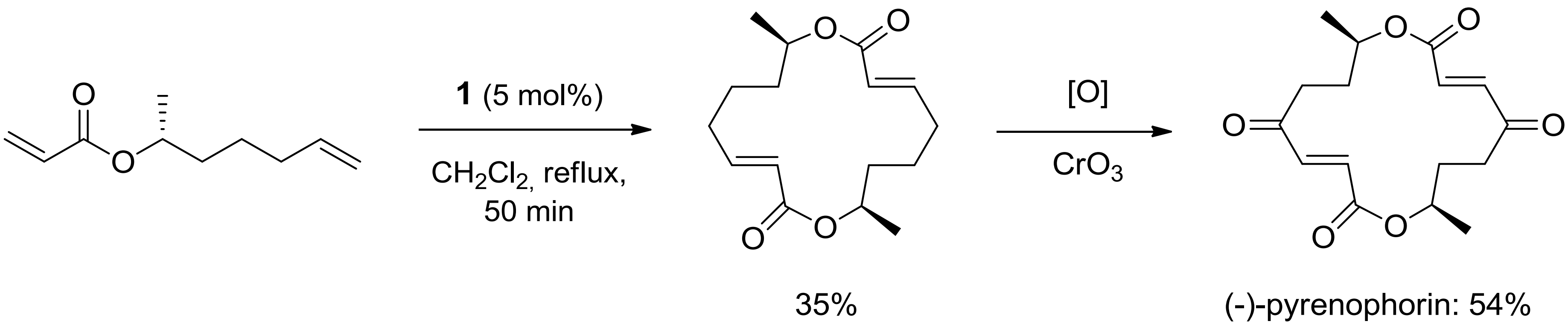


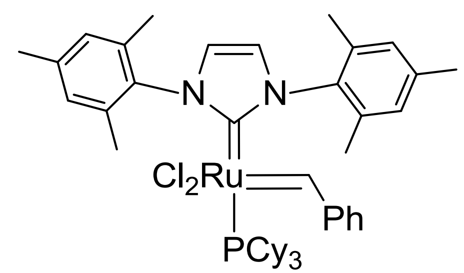
Ns = (o-NO_2)$C_6H_4SO_2$-

S. Blechert, *Org. Lett*. **2000**, *2*, 3971

Application to the synthesis of natural products

Synthesis of (*R*,*R*)-(-)-Pyrenophorin





1

A. Fürstner *Org. Lett*. **2001**, *3*, 449
for a new synthesis of epothilone A and C see:
A. Fürstner *Chem. Commun*. **2001**, 1057.

Olefin metathesis

Cross-/ self-metathesis with allylsilanes

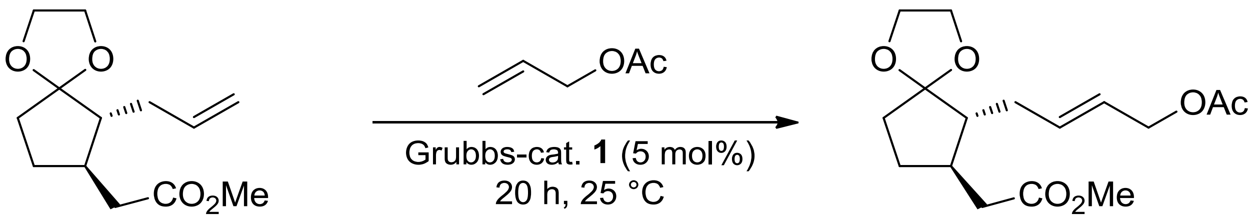
S. Blechert, *Chem. Eur. J*. **1997**, *3*, 441.

Cross-metathesis with allylic silyl ethers:
A.G.M. Barrett, *Chem. Commun*. **1996**, 2229 and 2231

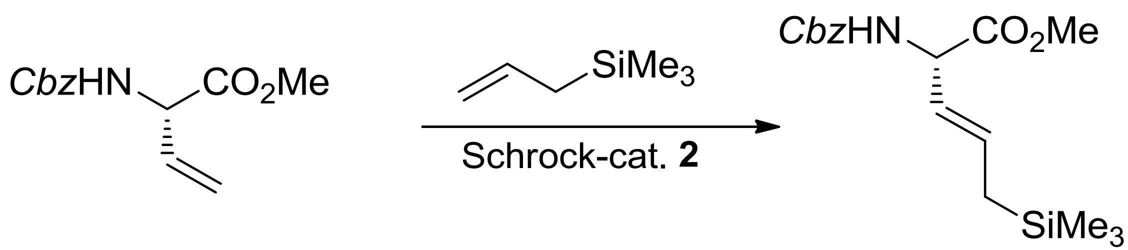
Cross-metathesis with fluorinated olefins:
S. Blechert, Chem. Commun. **2001**, 1692

Olefin metathesis

Synthesis of jasmonic acid derivatives



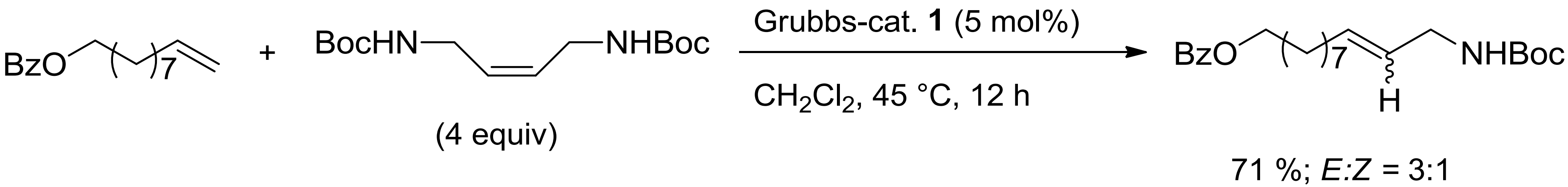
73 %



95 %, 95 %*ee*

S. Blechert, *Chem. Eur. J*. **1997**, *3*, 441
S.E. Gibson, *Chem. Commun*. **1997**, 1107
S. Blechert, *Chem. Commun*. **1997**, 1949

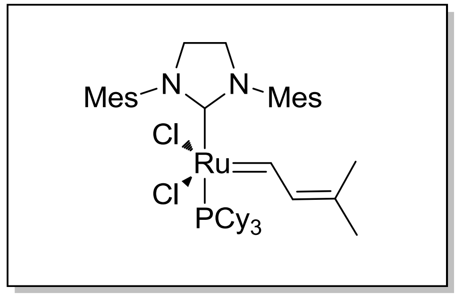
Olefin metathesis

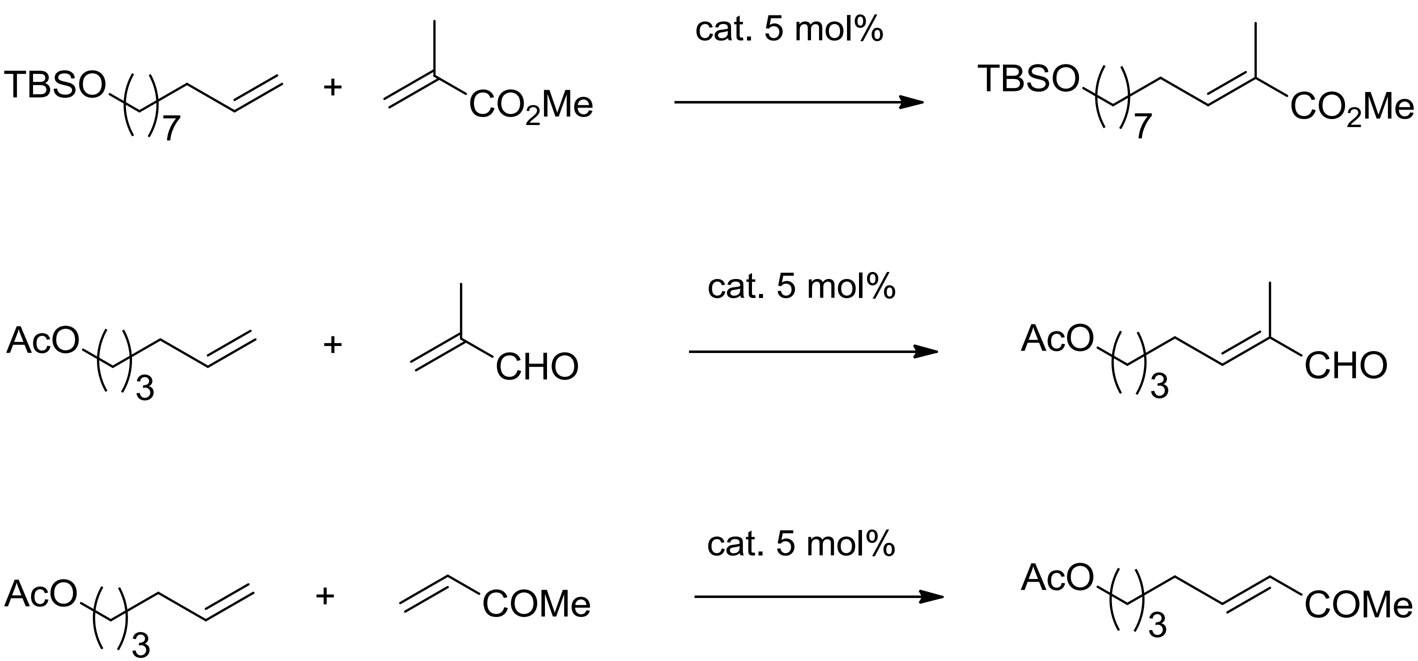


R.H. Grubbs, *Tetrahedron Lett*. **1998**, *39*, 7427

Olefin metathesis

Cross-metathesis using a mixed metathesis-catalyst





62 % *E* / *Z* > 20 : 1

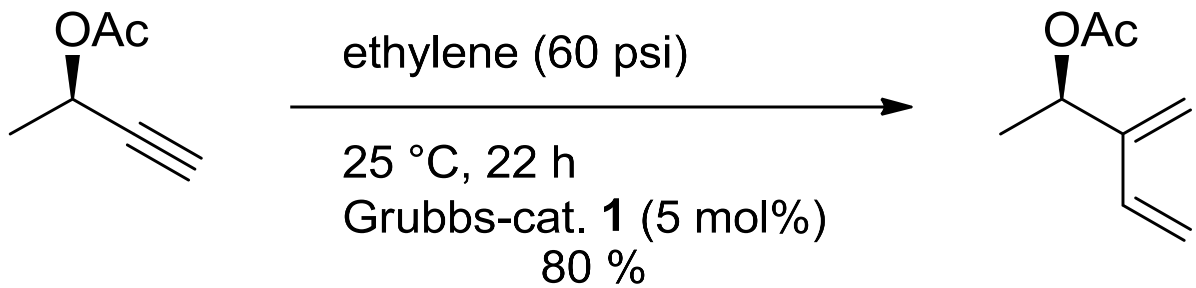
92 % *E* / *Z* > 20 : 1

95 % *E* / *Z* > 20 : 1

R. H. Grubbs, *J. Am. Chem. Soc*. **2000**, *122*, 3783

Olefin metathesis

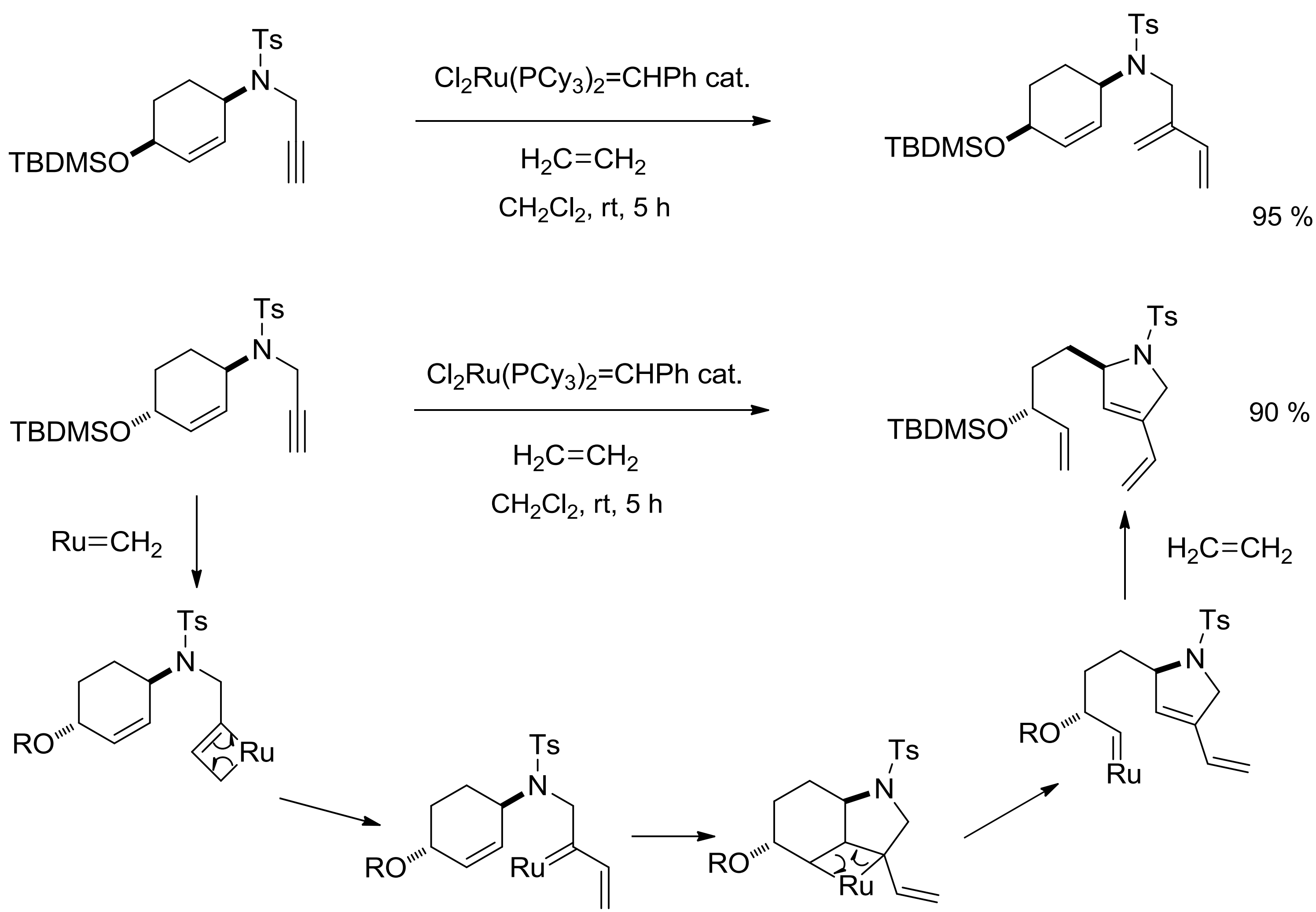
Cross-metathesis of alkynes with ethylene



S.T. Diver, *J. Org. Chem*. **2000**, *2*, 1788

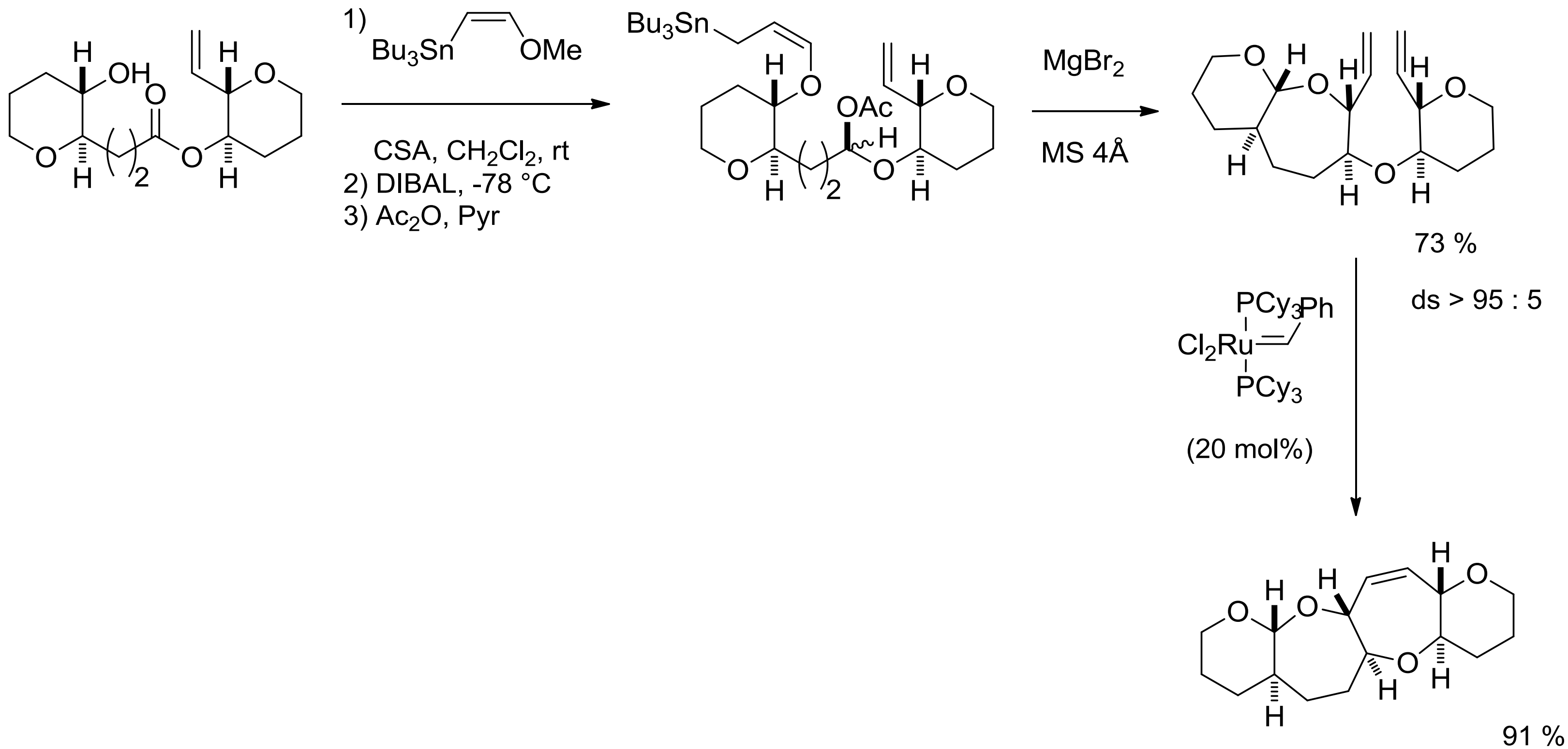
Olefin metathesis

Ru-catalyzed Ring-Opening and –Closing Enyne Metathesis



Olefin metathesis

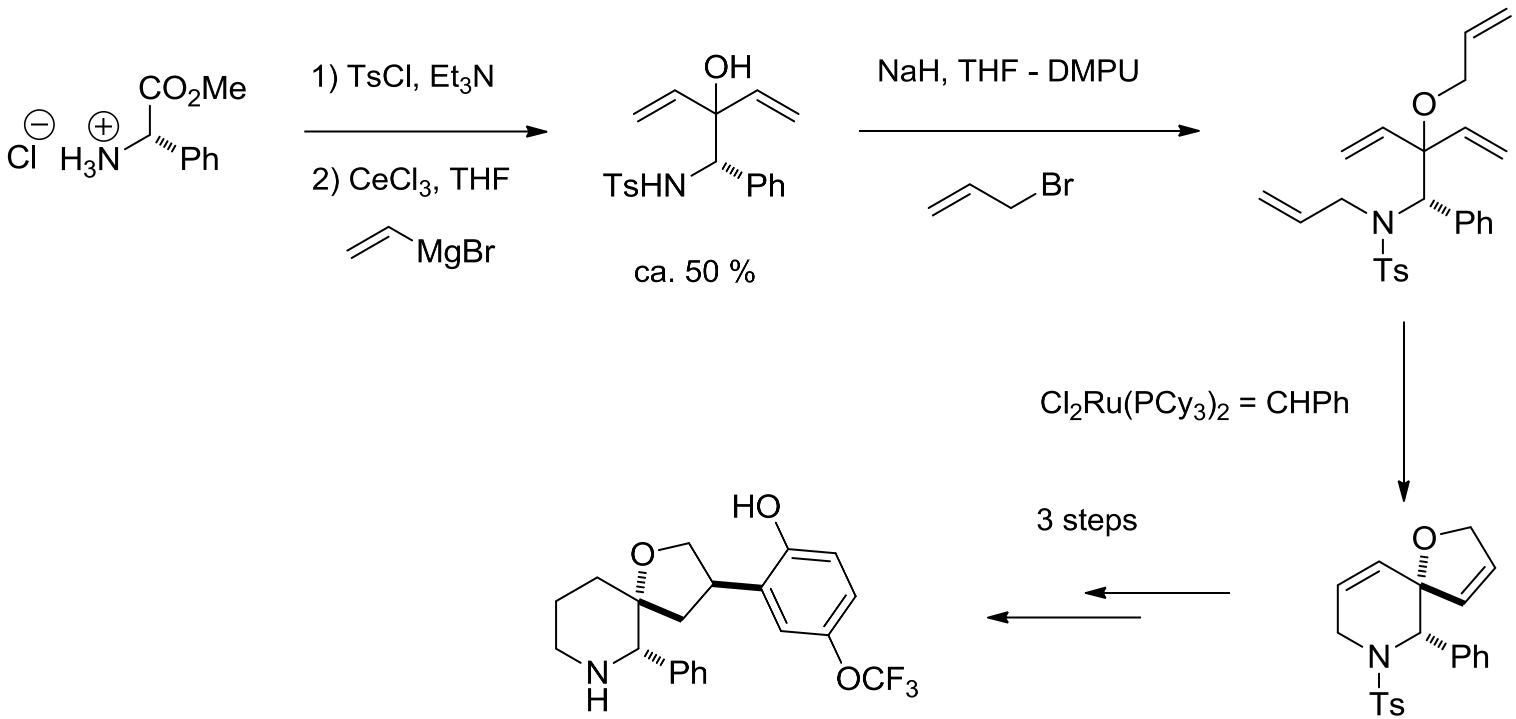
Synthesis of complex ring-systems *via* metathesis



Y. Yamamoto, *J. Am. Chem. Soc*. **2001**, *123*, 6702

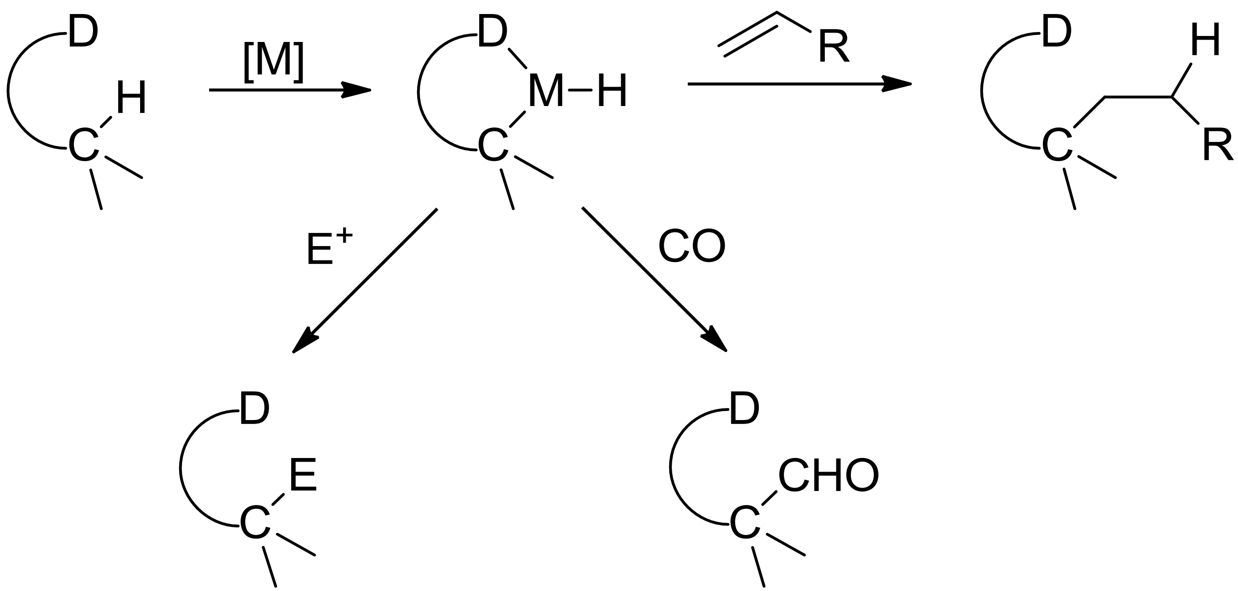
Olefin metathesis

A double ring closing metathesis for the synthesis of NK-1 receptor antagonists



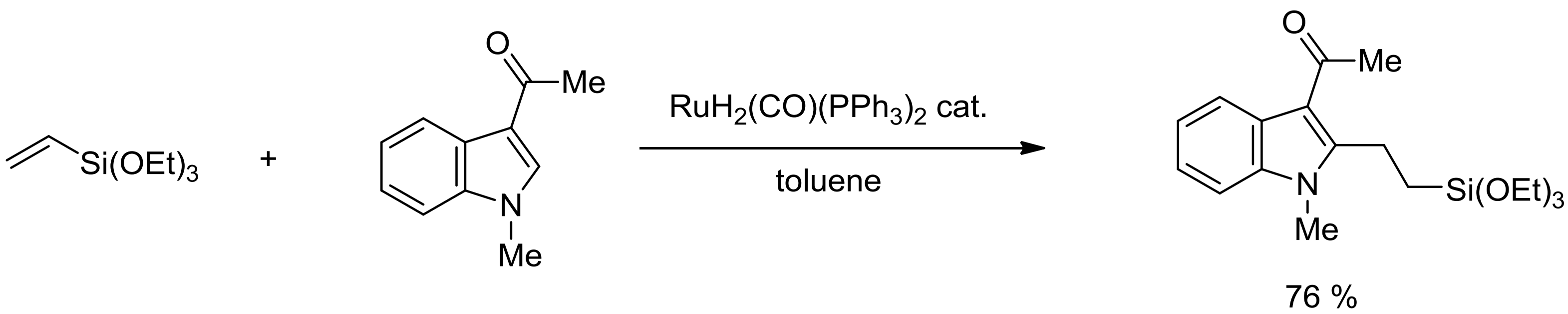
Merck-team *Org. Lett*. **2001**, *3*, 671

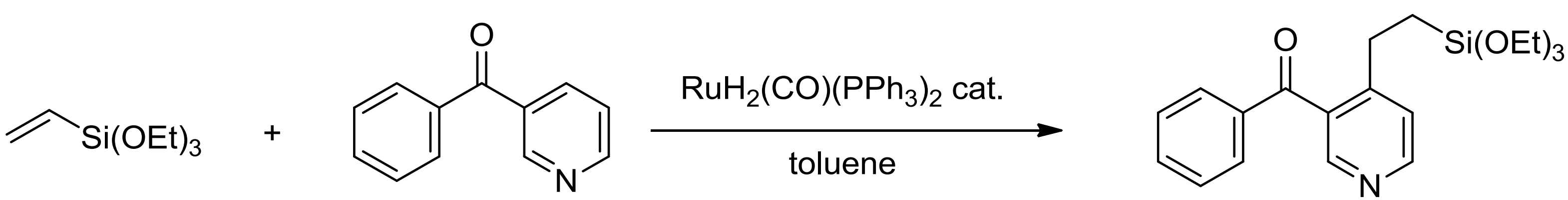
New C-H activation reactions



Book: S. Murai, (Ed.) Activation of Unreactive C-H Bonds in Organic Synthesis, Topics in Organometallic Chemistry, Springer, **1999**.

The Murai-reaction

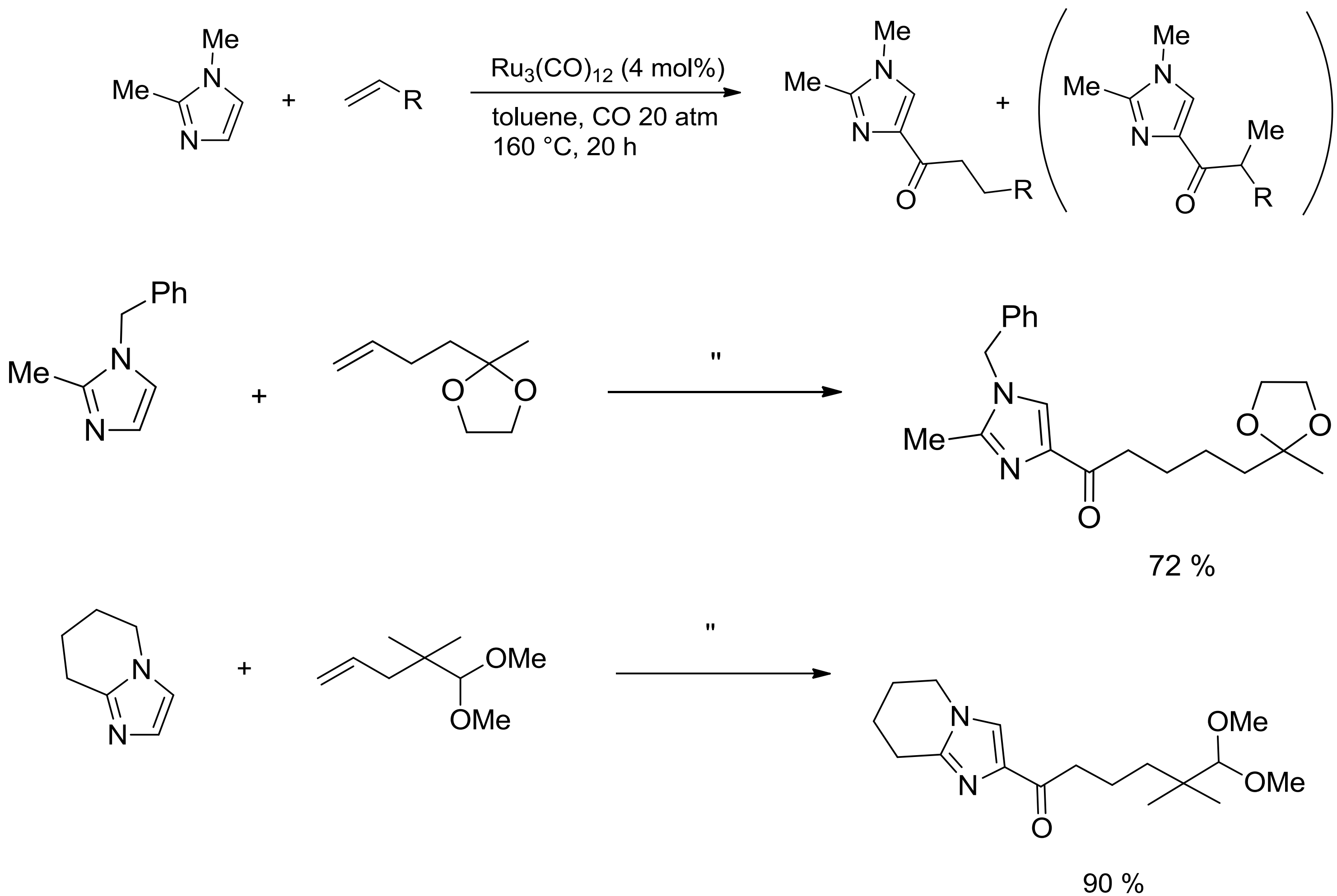




R. Grigg, *Tetrahedron Lett*. **1997**, *38*, 5737
S. Murai, *Nature*, **1993**, *366*, 529
S. Murai, *J. Organomet. Chem*. **1995**, *504*, 151

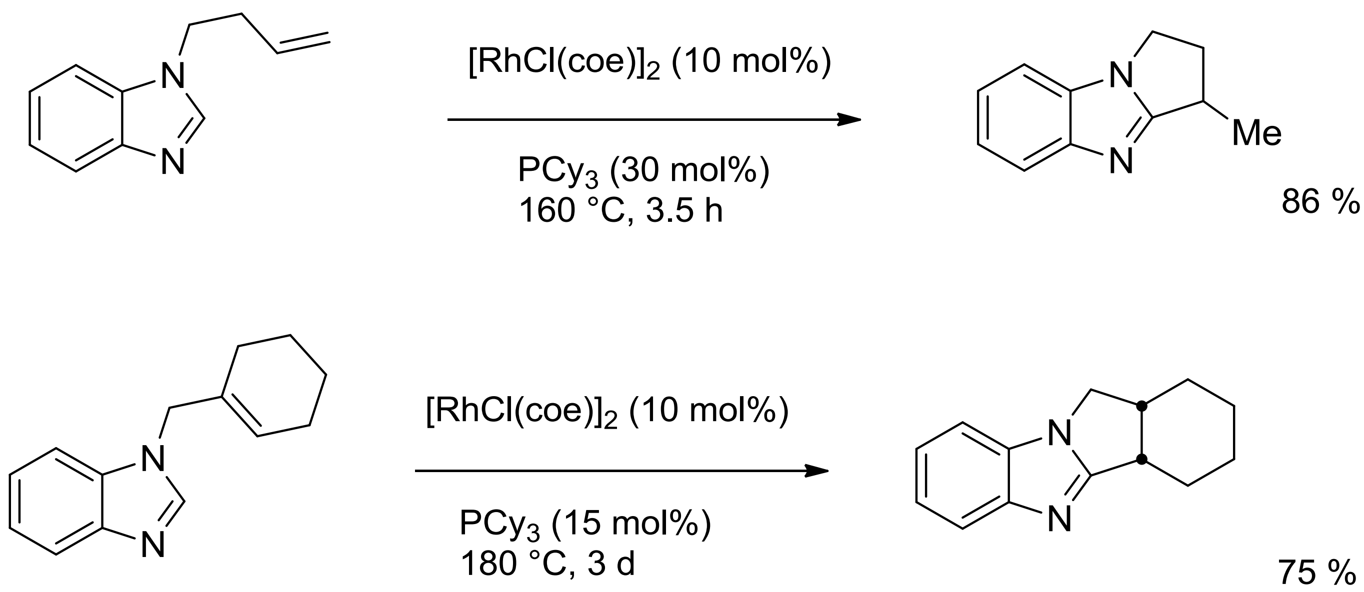
The Murai-reaction

Ru-mediated synthesis of 4-acylated imidazoles *via* C-H-activation



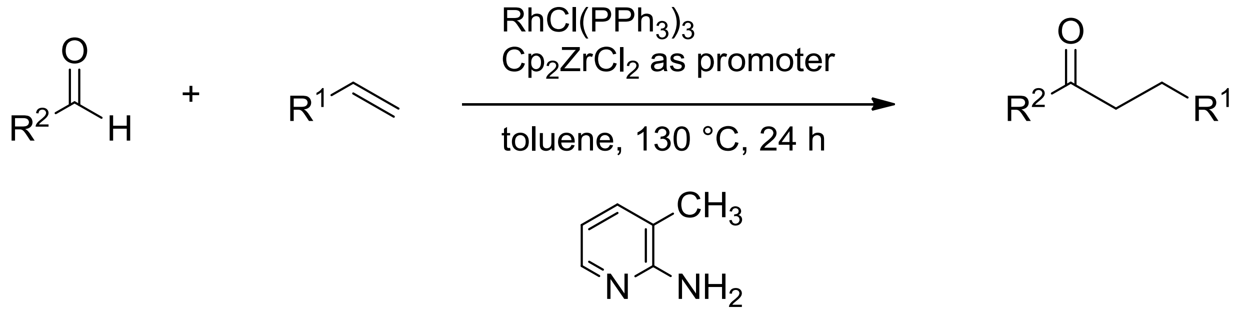
S. Murai, *J. Am. Chem. Soc*. **1996**, *118*, 493

Annulation of heterocycles *via* a Rh-catalyzed C-H-activation

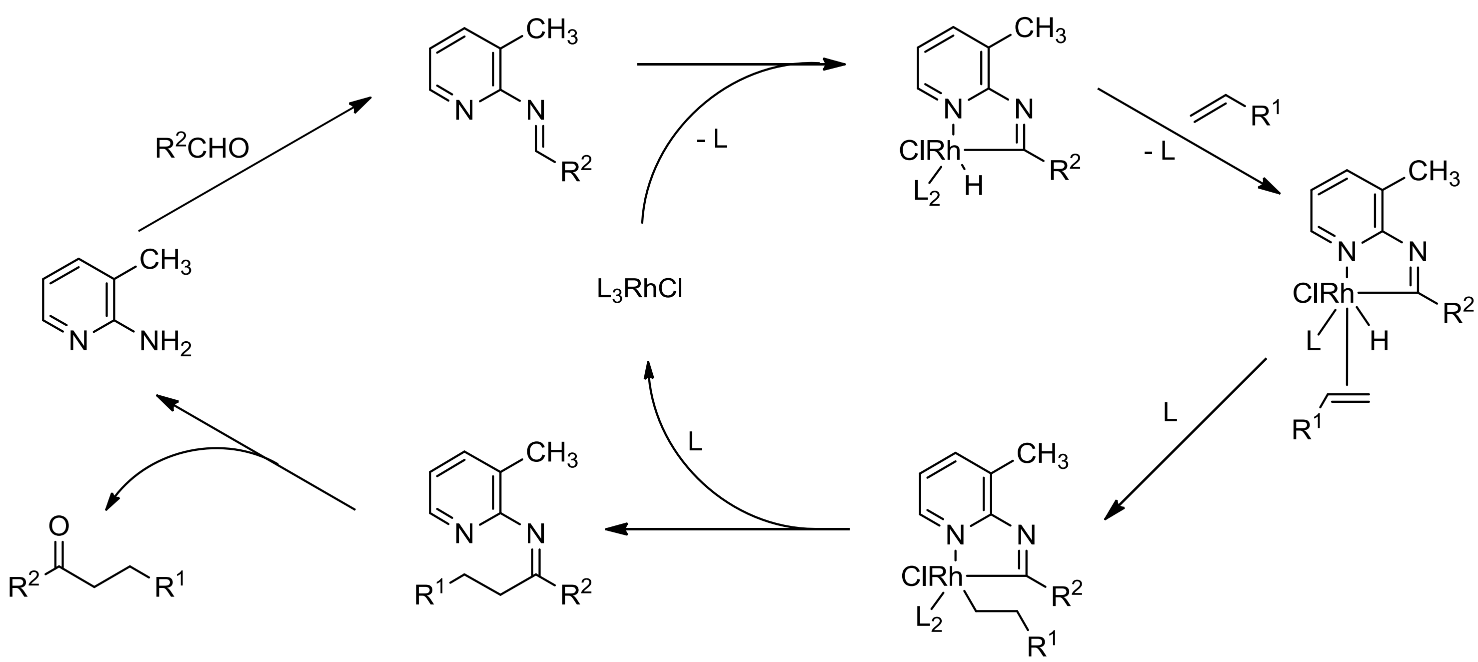


R. G. Bergman, J. Ellman, A. *J. Am. Chem. Soc*. **2001**, *123*, 2685

The catalytic hydroacylation of alkenes



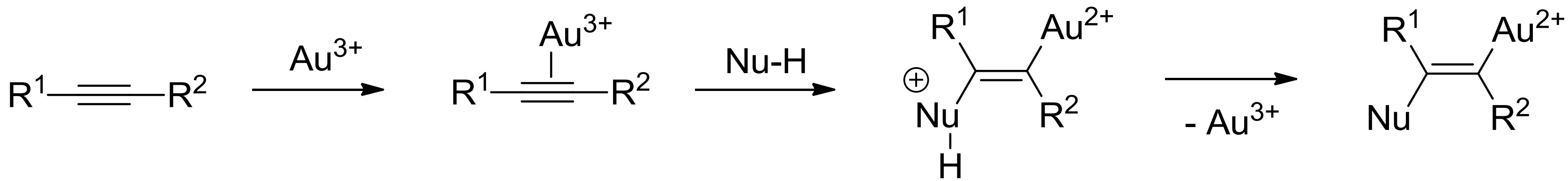
Mechanism:

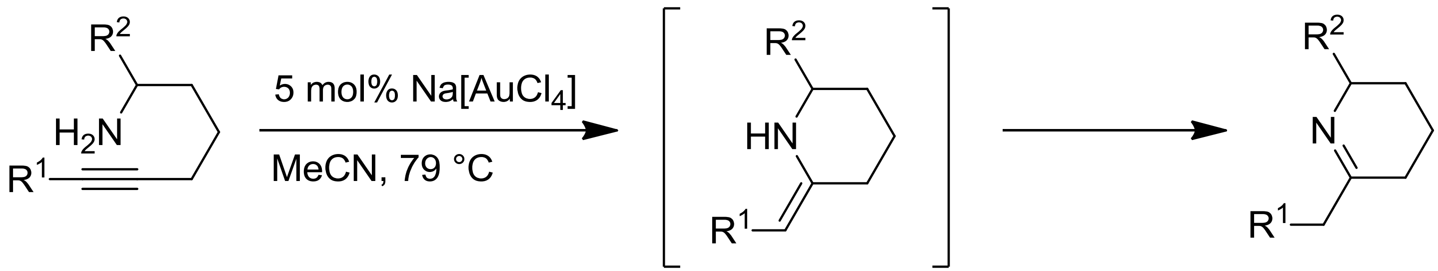


Review: C.-H. Jun, *Synlett*, **1999**, 1
C.-H. Jun, *Org. Lett*. **1999**, *1*, 887; *Tetrahedron Lett*. **1997**, *38*, 6673; *J. Org. Chem*. **1997**, *62*, 1200

Gold-catalyzed organic reactions

Nucleophilic addition to C-C multiple bonds



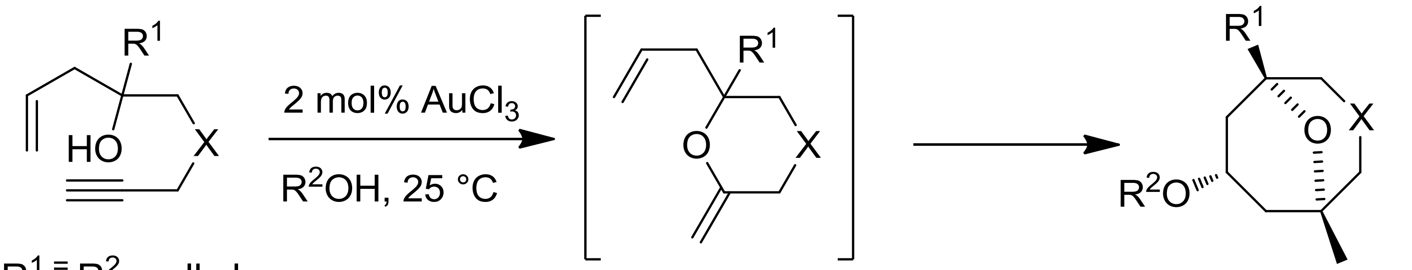


For a review see: A. S. Hashmi, *Chem. Rev*. **2007**, *107*, 3180

Gold-catalyzed organic reactions

Nucleophilic addition to C-C multiple bonds:

Au^{3+}-catalyzed cyclization followed by a Prins type cyclization



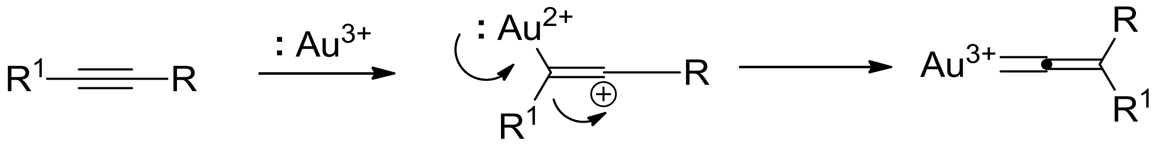
R1 = R2 = alkyl
X = CH2, O

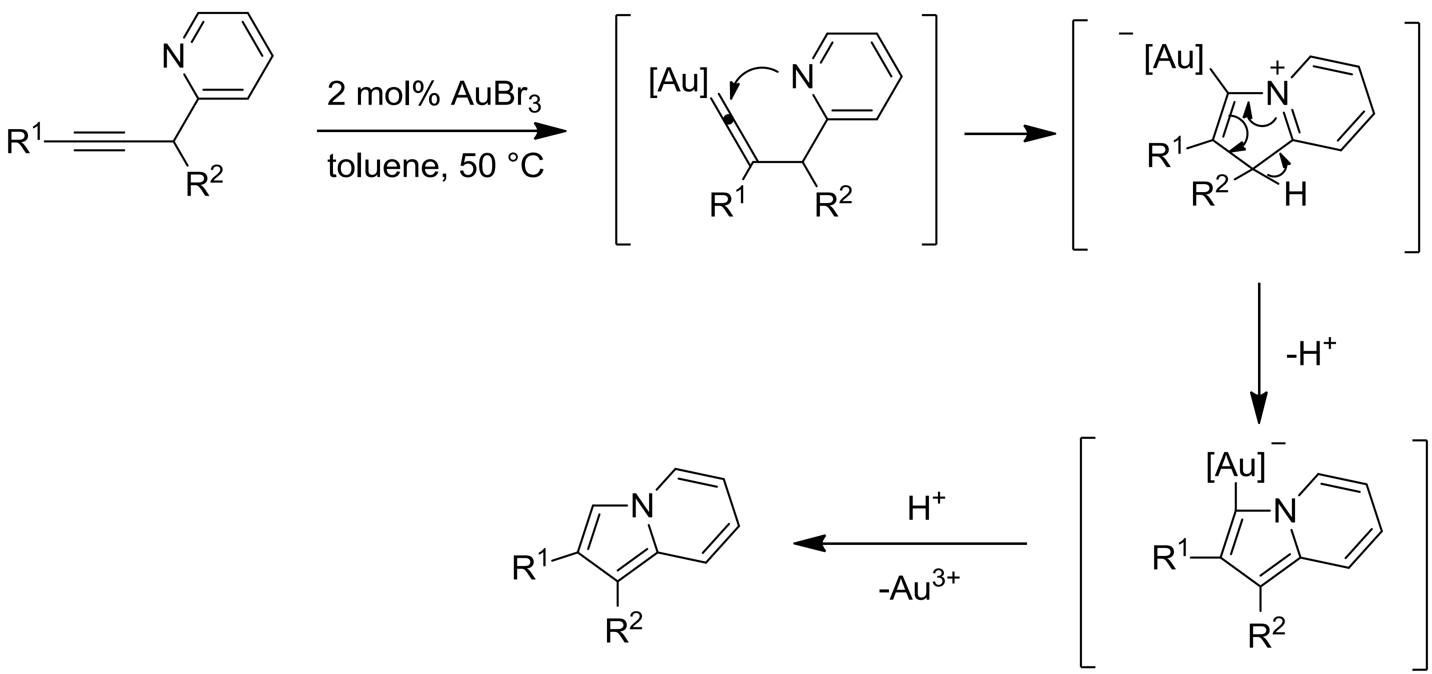
88-96%

For a review see: A. S. Hashmi, *Chem. Rev*. **2007**, *107*, 3180

Gold-catalyzed organic reactions

Gold(III)-triggered rearrangements

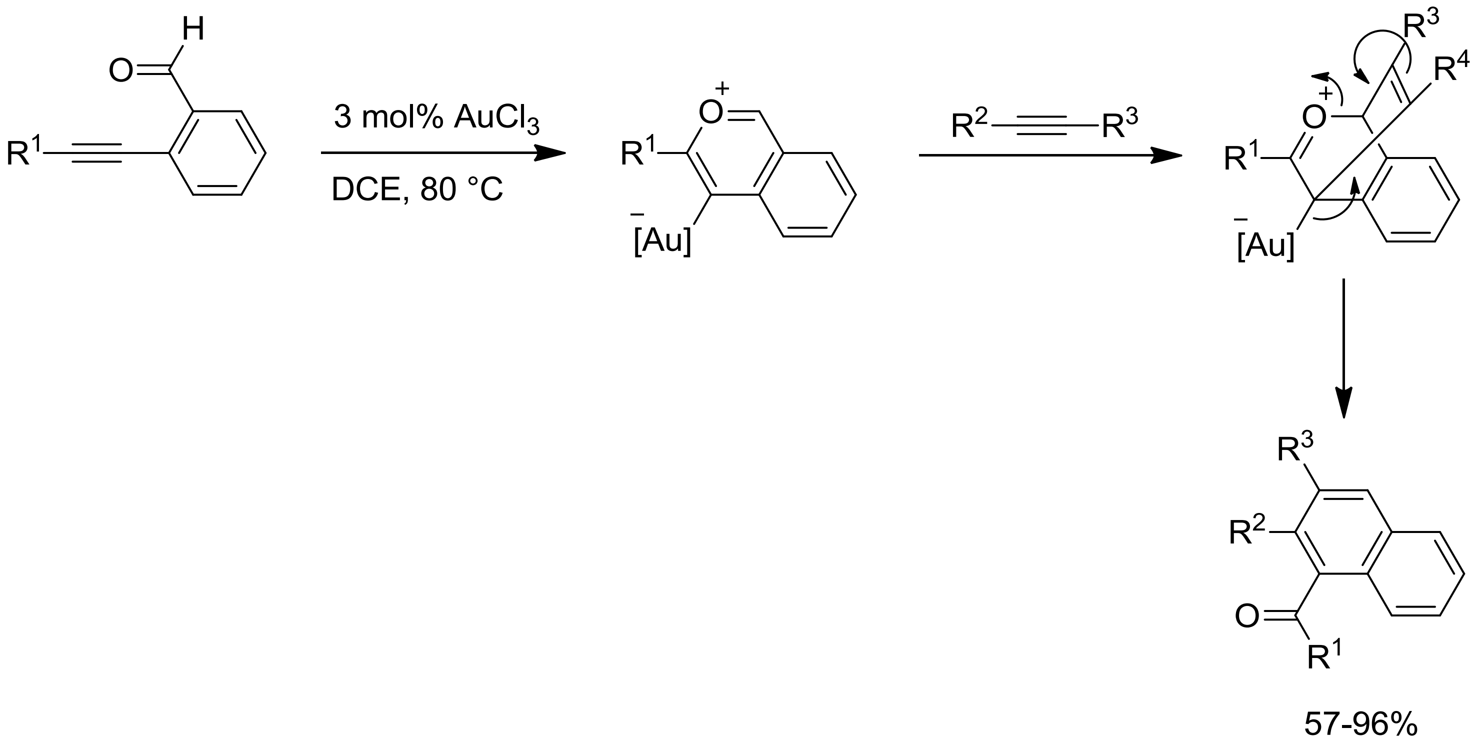




35-96%

Gold-catalyzed organic reactions

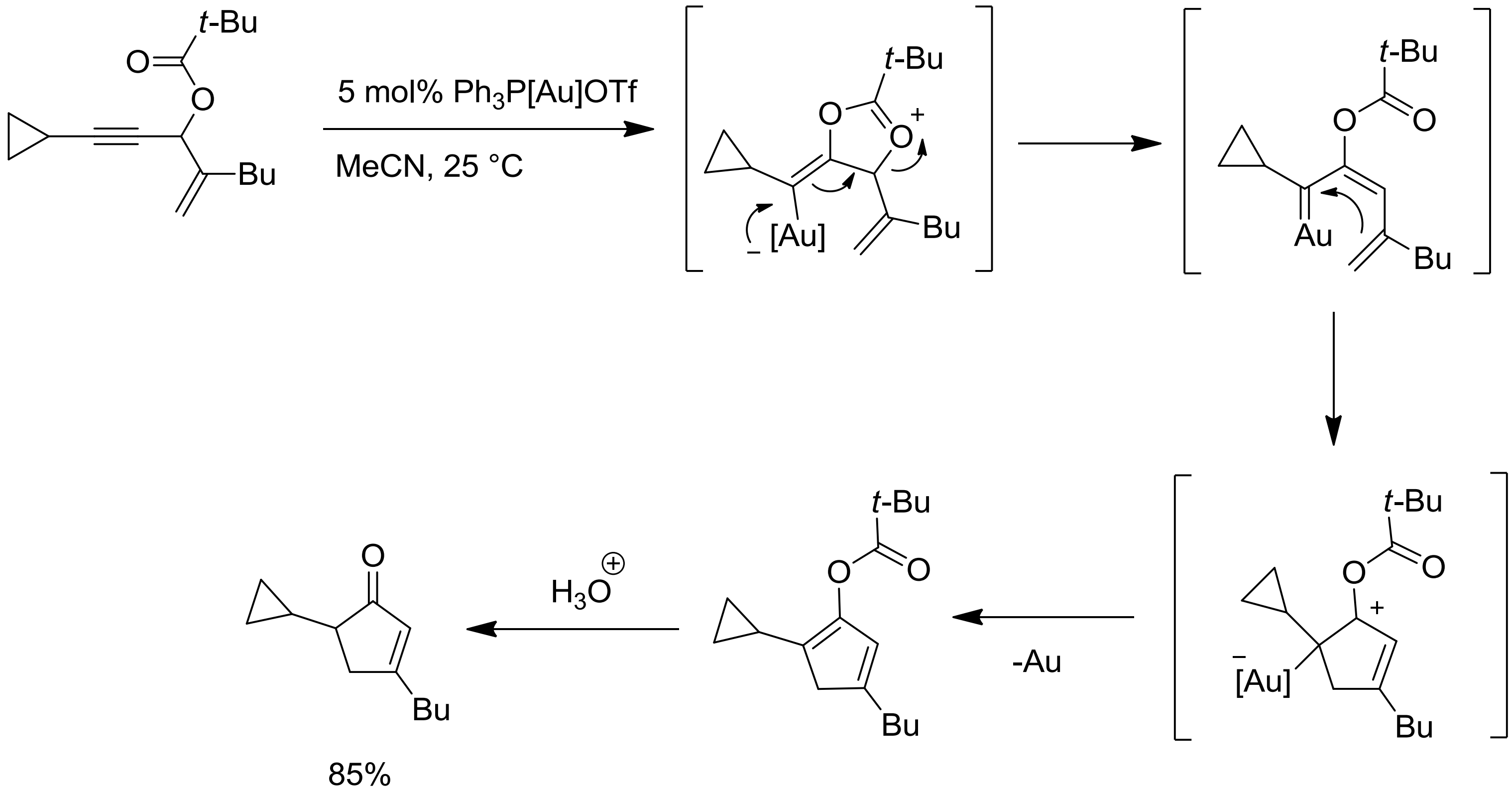
Au^{3+}-initiated cycloadditions



Y. Yamamoto, *J. Am. Chem. Soc*. **2003**, *125*, 10921

Gold-catalyzed organic reactions

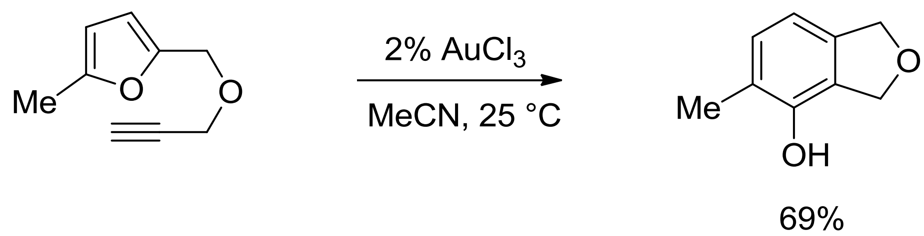
Use of electrophilic Gold(I)-complexes: Ph_3P-Au-OTf

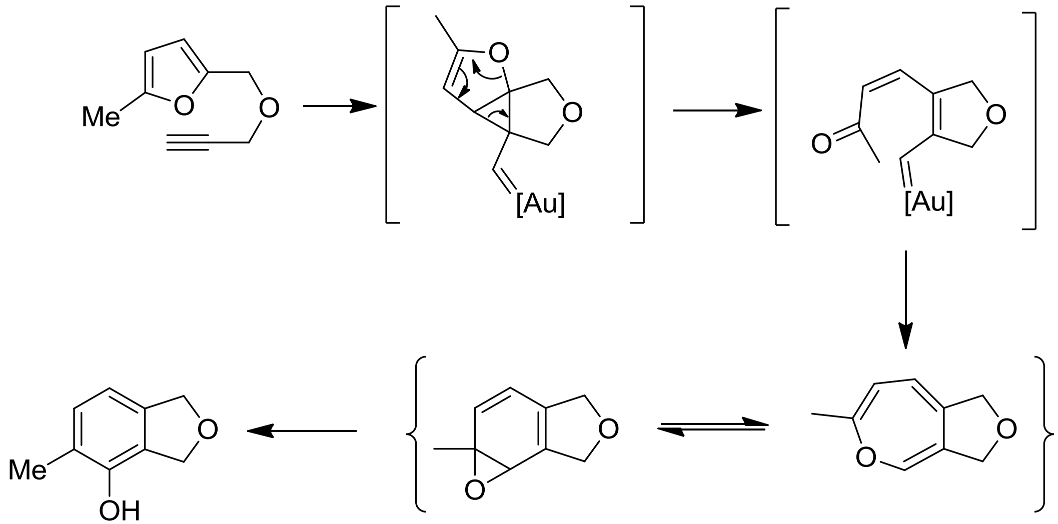


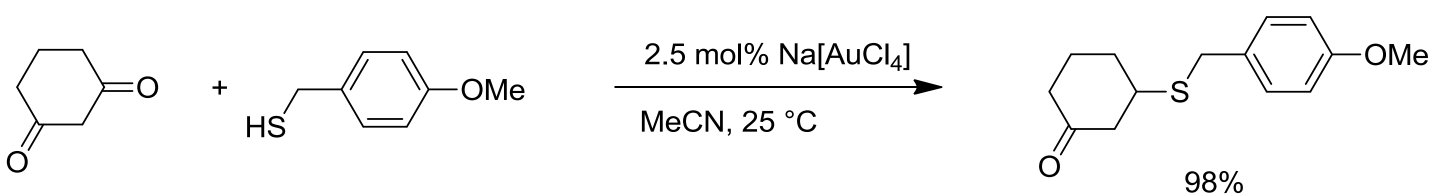
F. D. Toste *J. Am. Chem. Soc*. **2005**, *127*, 5802

Gold-catalyzed organic reactions

Intramolecular phenol synthesis



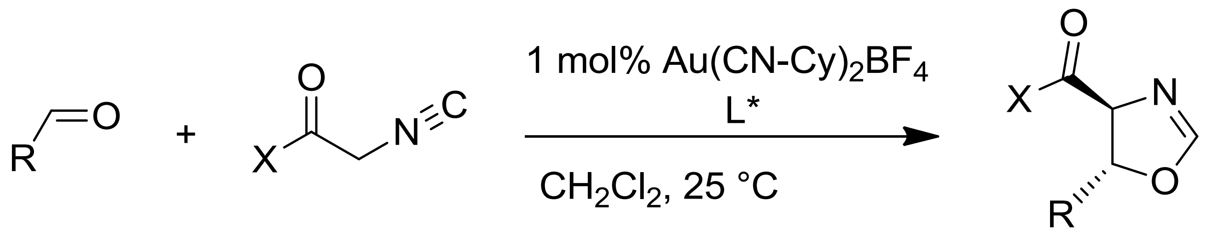




A. S. Hashmi, *J. Am. Chem. Soc*. **2000**, *122*, 11553

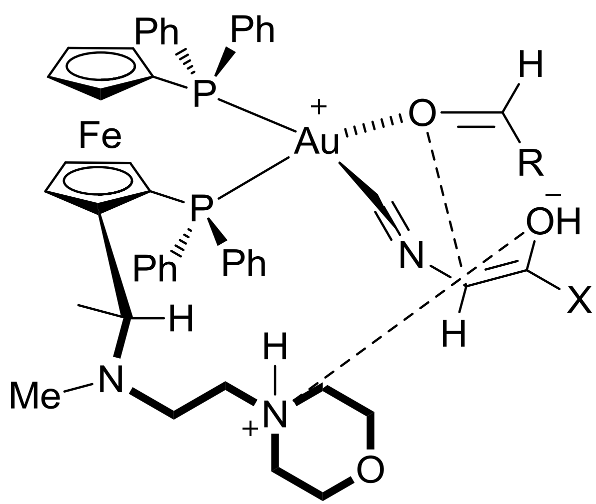
Gold-catalyzed organic reactions

Asymmetric aldol reaction



86-97%

trans : *cis* up to 93 : 7
up to 94% ee



T. Hayashi *J. Am. Chem. Soc*. **1986**, *108*, 6405