# *Allenes as Products, Substrates, or Intermediates in Organometallic Transformations*

**August 23, 2006**

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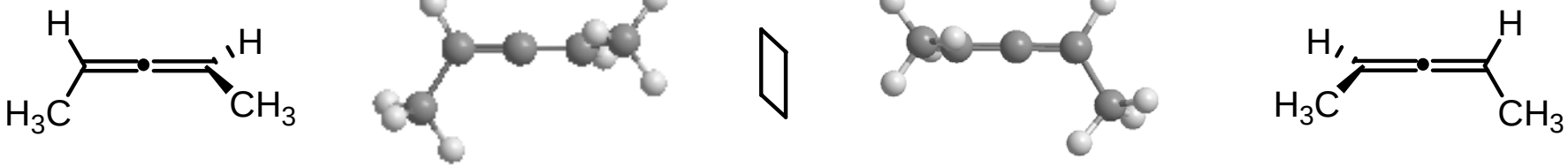
**The Sorensen Group, Department of Chemistry**

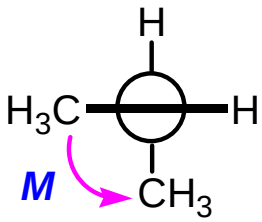
## Chirality of Allene



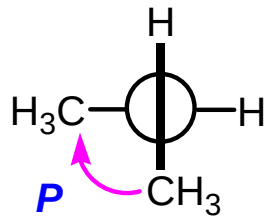

(*M*)-2,3-pentadiene

(*P*)-2,3-pentadiene

**Stereogenic Axis**




**Counter-clockwise**



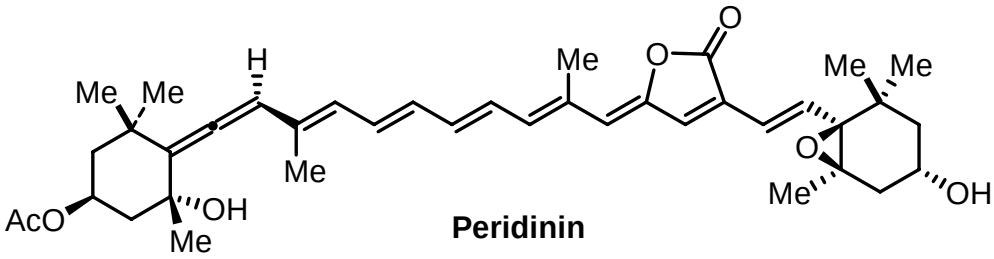

**Clockwise**

***Allenes*: 1,2-dienyl compounds with stereogenic axis**

**In 1875, Van't Hoff had expected an allene structure**

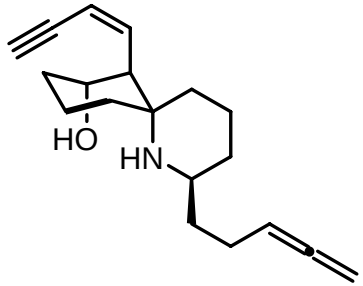
**In 1887, Burton and von Pechmann reported the first documented synthesis**

## Representative natural products containing an allene moiety

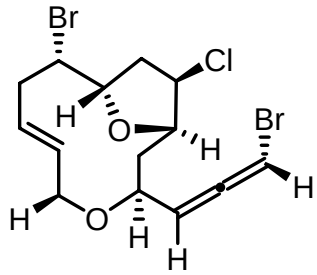



**Peridinin**

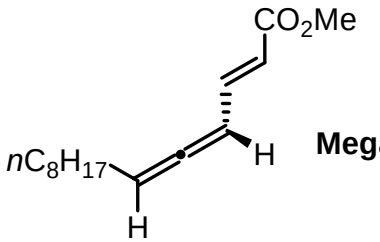
isolation 1890; structure 1971; synthesis 2002



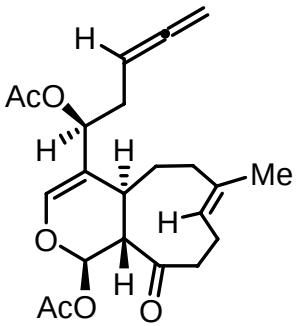

**Isodihydrohistrionicotoxin**



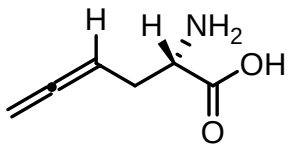

**Obtusallene**



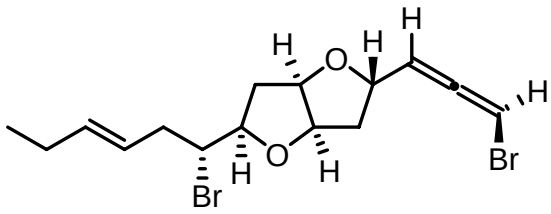

**Megatomoic Methyl Ester**



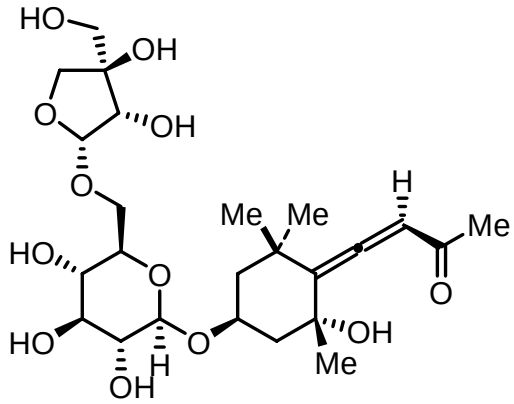

**Ginamallene**




**4,5-Dienoic aminoacid**




**Kumausallene**

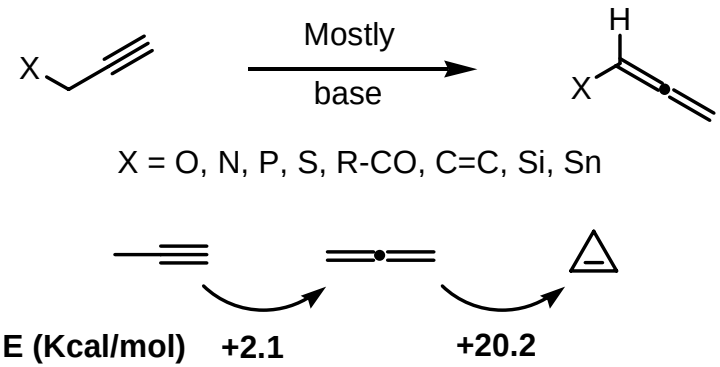



**Cinnamoside**

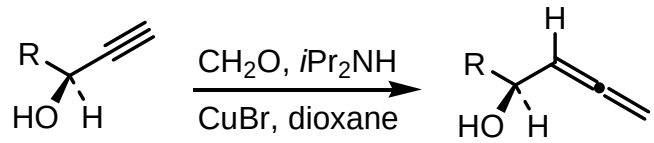
Hoffmann-Roder, A.; Krause, N. *Angew. Chem. Int. Ed.* **2004**, *43*, 1196.

# Preparation Methods

## Isomerization Reactions

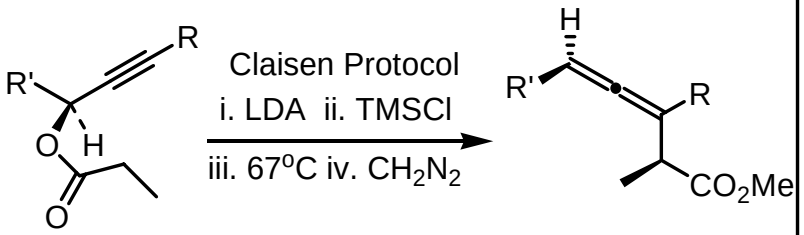



## Crabbe Homologative Allenylation



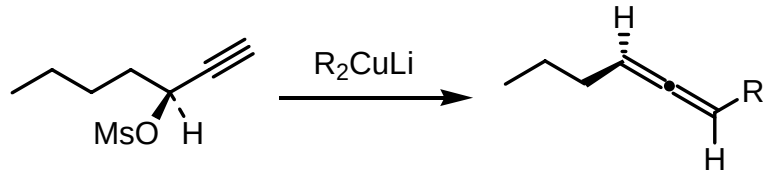

**Simple trial with many functional groups tolerance**

## Sigmatropic Rearrangements




**A variety of [2,3]-Wittig, [2,3]-Sigmatropics are well established**

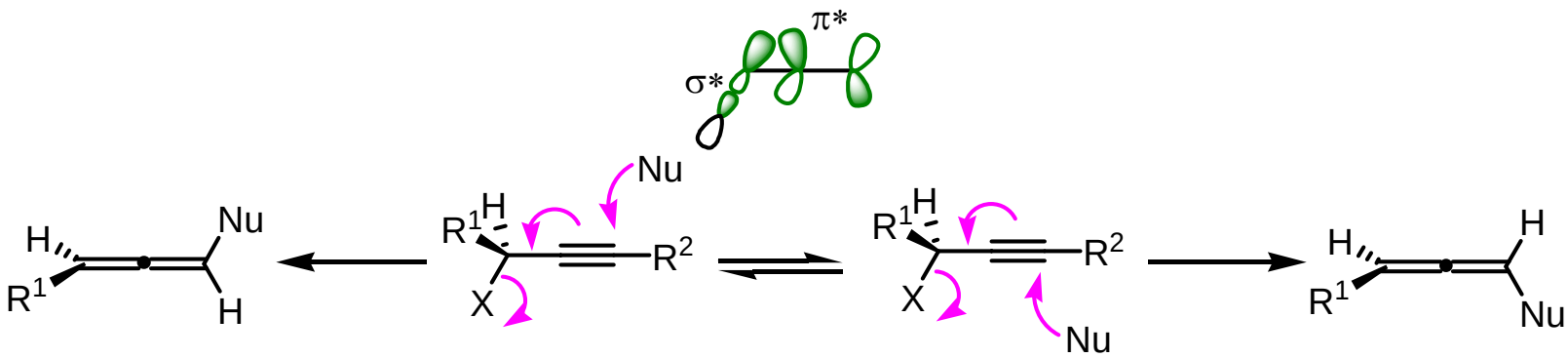
## Metal Mediated $S_N2'$ Type Substitutions




**Various nucleophiles and metals have been utilized for this transformation**

# π-Facial Aspects of $S_N2'$

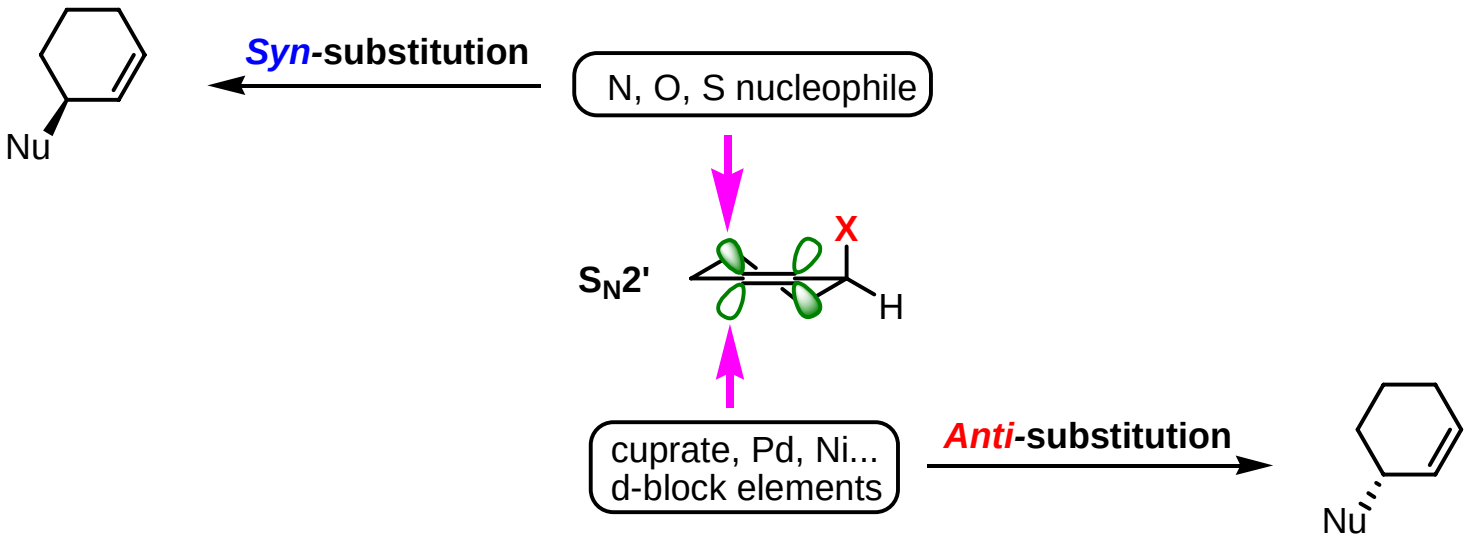
## Self-immolative chirality trasfer from center to axis chirality



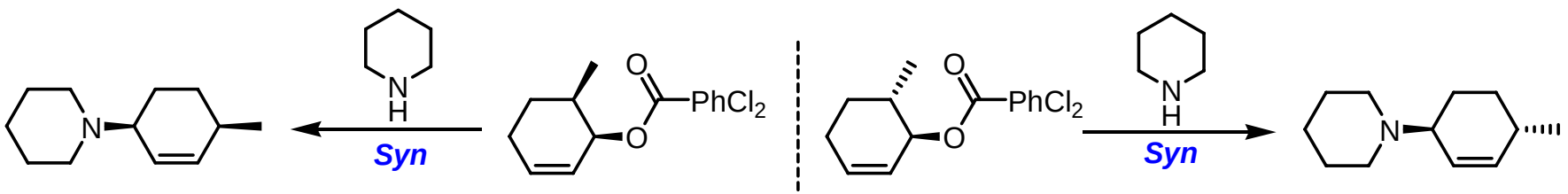

***anti*-mode** **syn-mode**

**Both modes are stereoelectronically allowed**

## In general,

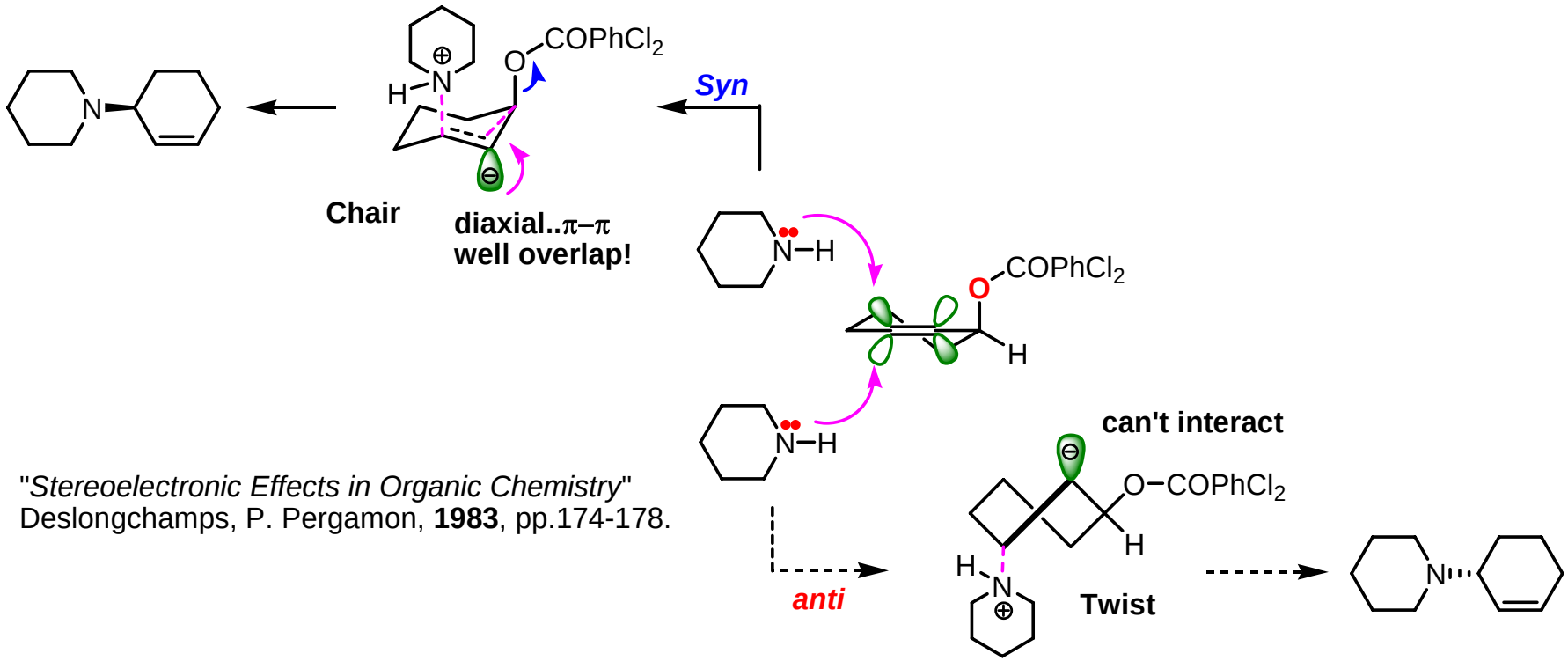


# *Syn* $S_N2'$ Displacement




Stork, G. et al., *J. Am. Chem. Soc.* **1953**, *75*, 4119; **1977**, *99*, 3850

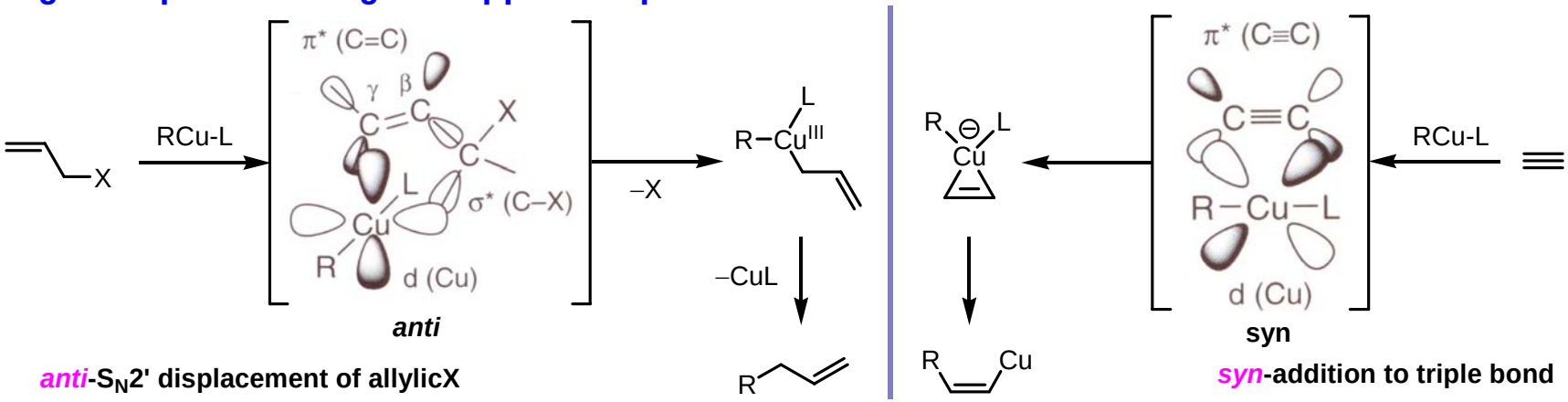
## Mechanistic Aspects of Syn $S_N2'$ Reaction




"*Stereoelectronic Effects in Organic Chemistry*"
Deslongchamps, P. Pergamon, **1983**, pp.174-178.

# *Anti* $S_N2'$ Displacement

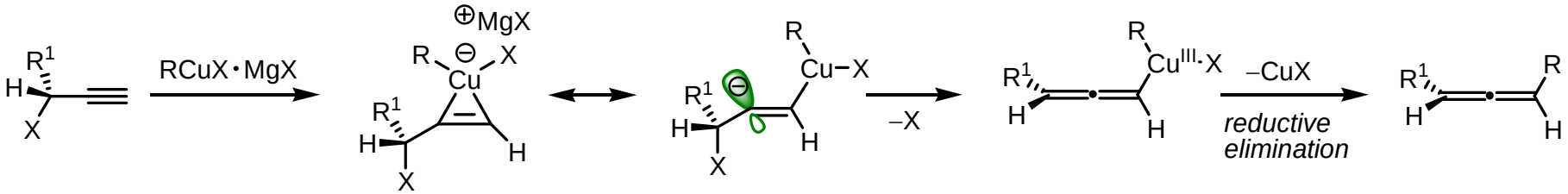
## Organocuprate and Organocopper Compounds

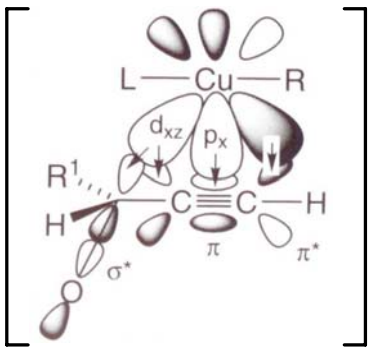



***anti*-$S_N2'$ displacement of allylicX** | ***syn*-addition to triple bond**

**Combine**

**Mechanistic Behavior of anti-$S_N2'$ substitution of Proparylic X**

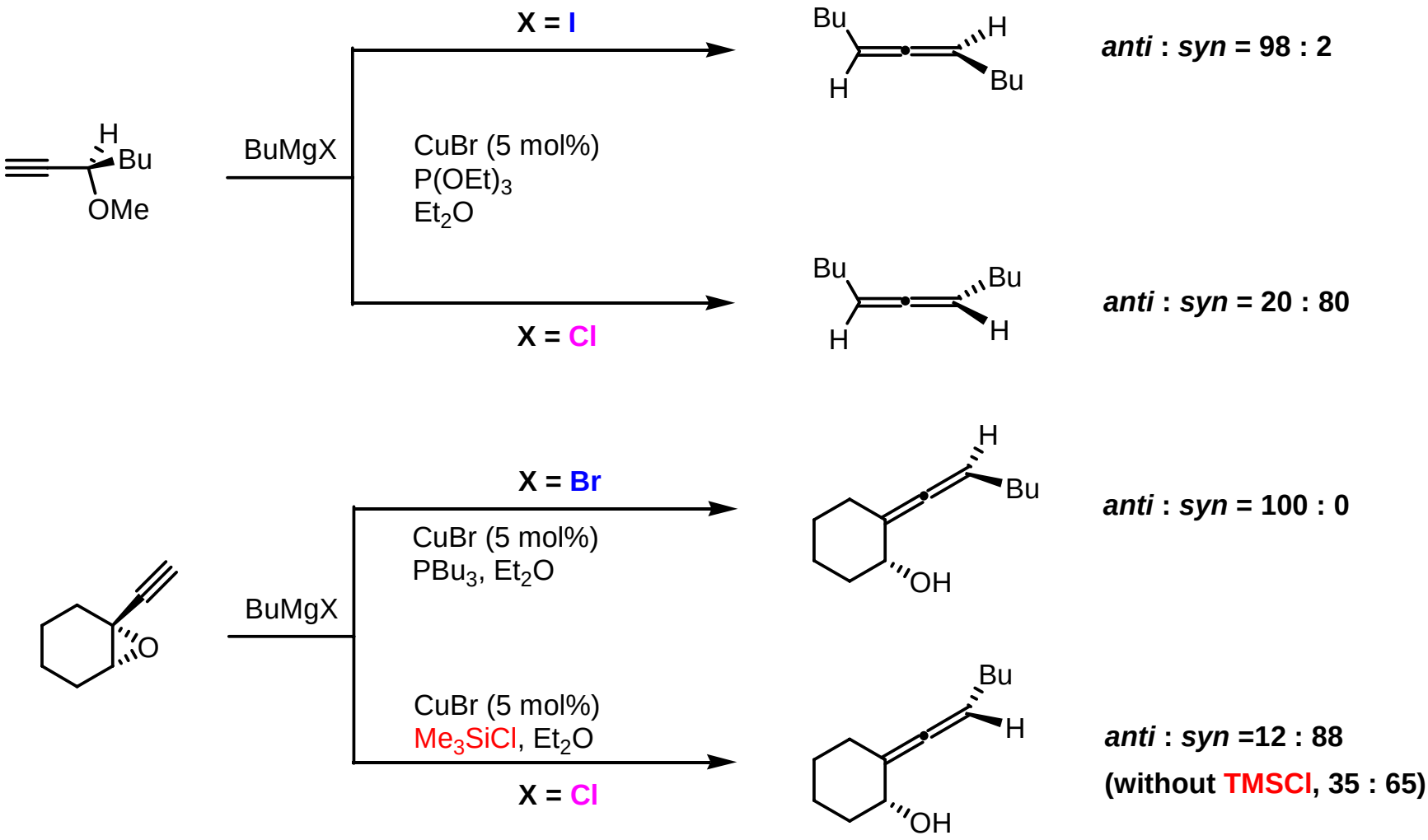




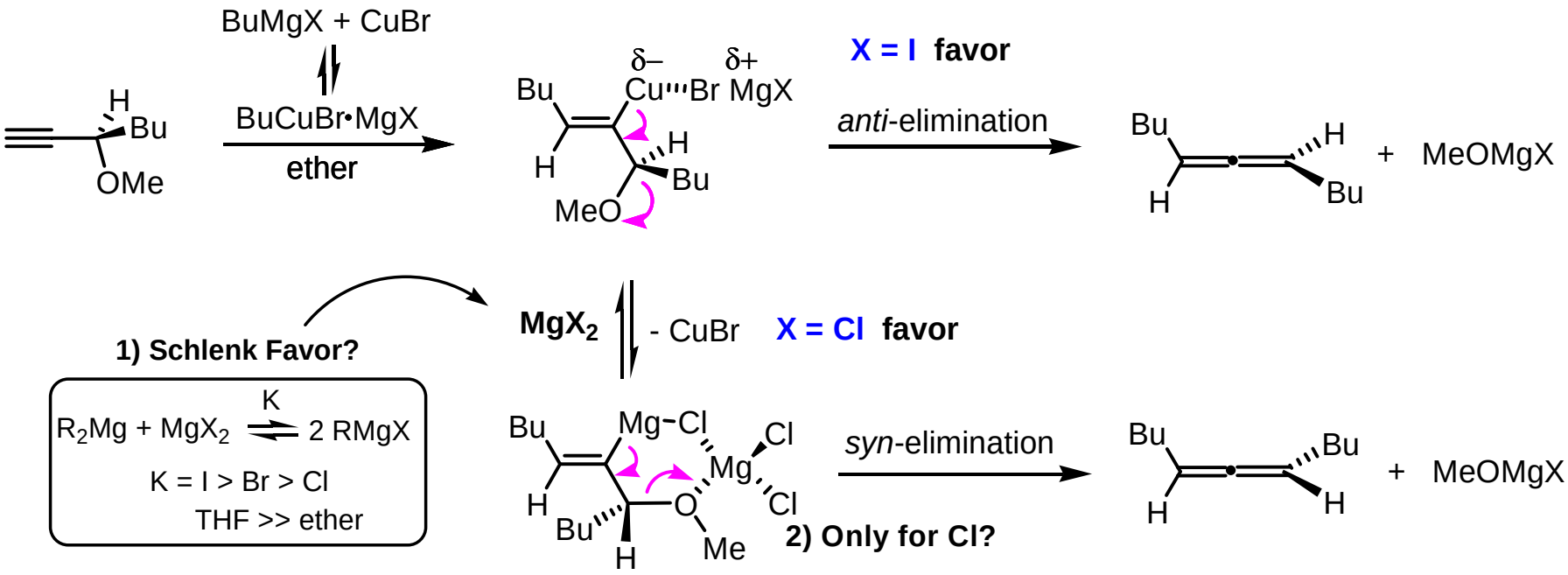
Corey, E. J.; Boaz, N. W. *Tetrahedron Lett*. **1984**, 25, 3063.
Elsevior, C. J.; Vermer, P. *J. Org. Chem.* **1989**, *54*, 3726.
Krause, N. Ed., "*Mordern Organocopper Chemistry*" Wiley-VCH, **2002**.

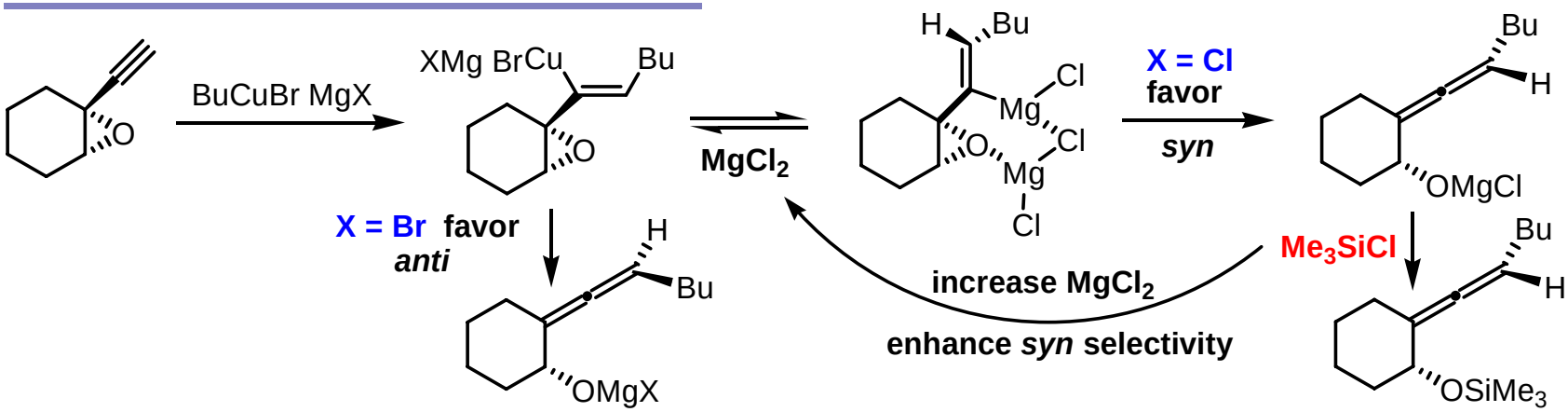
# *Anti* vs *Syn* Selectivity



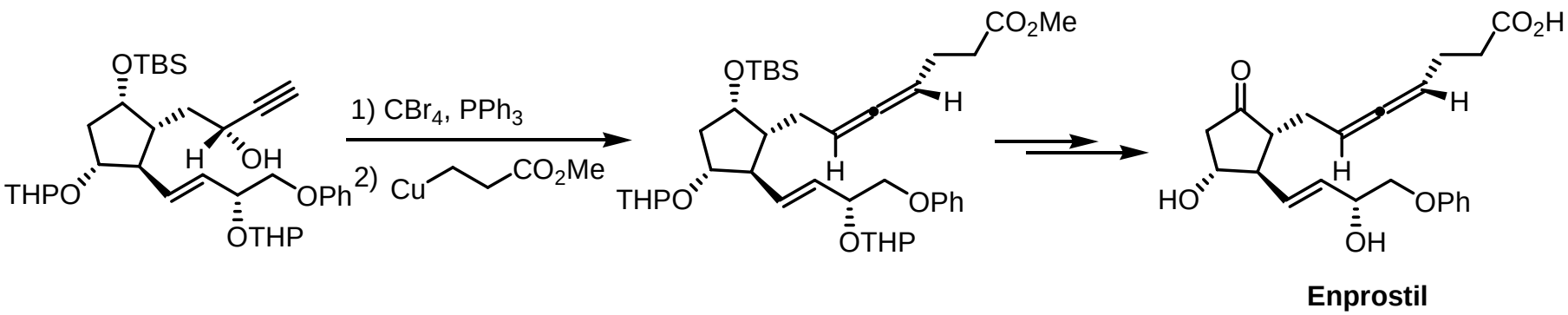

Alexakis, A. et al. *J. Am. Chem. Soc.* **1990**, *112*, 8042; *Tetrahedron* **1991**, *47*, 1677.

# Plausible Pathways



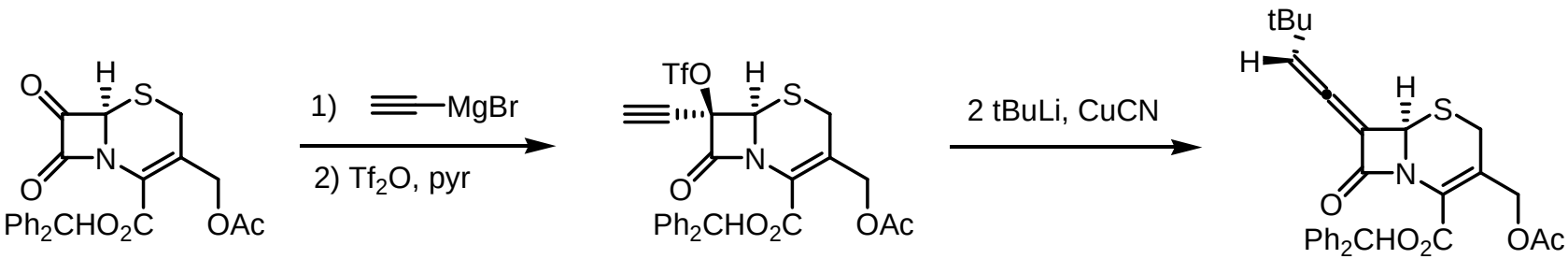



# $S_N2'$: C-C Bond Formation



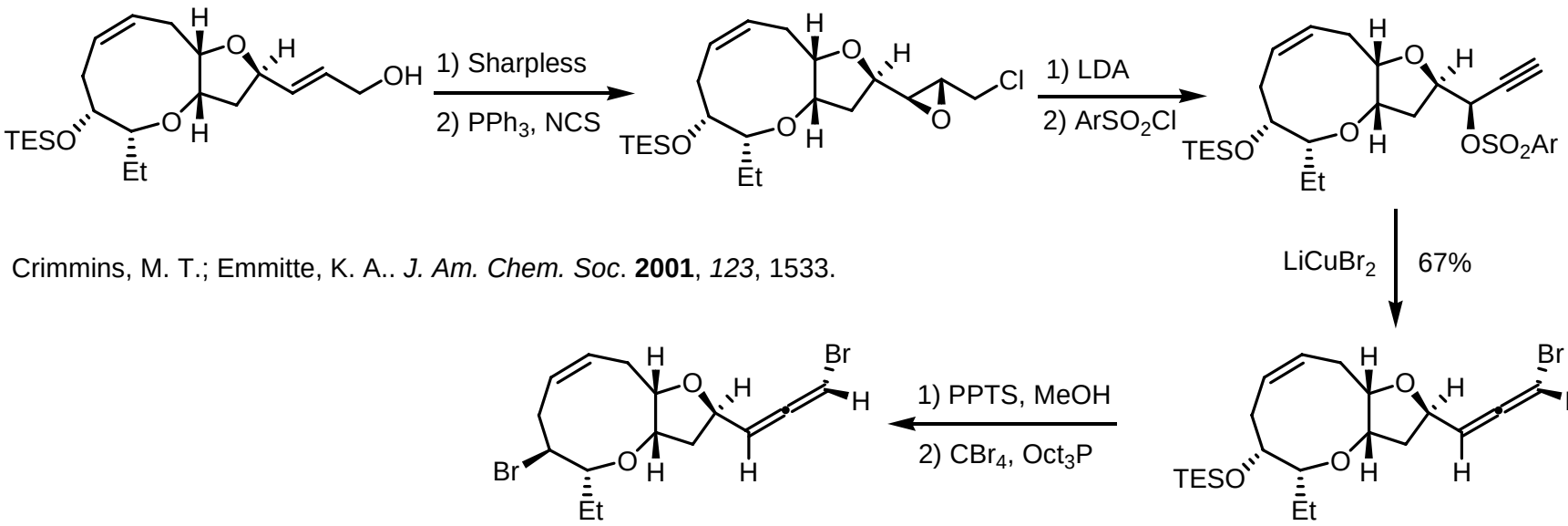

**Enprostil**

Cooper, G. F. et al. *J. Org. Chem*. **1993**, *58*, 4280.



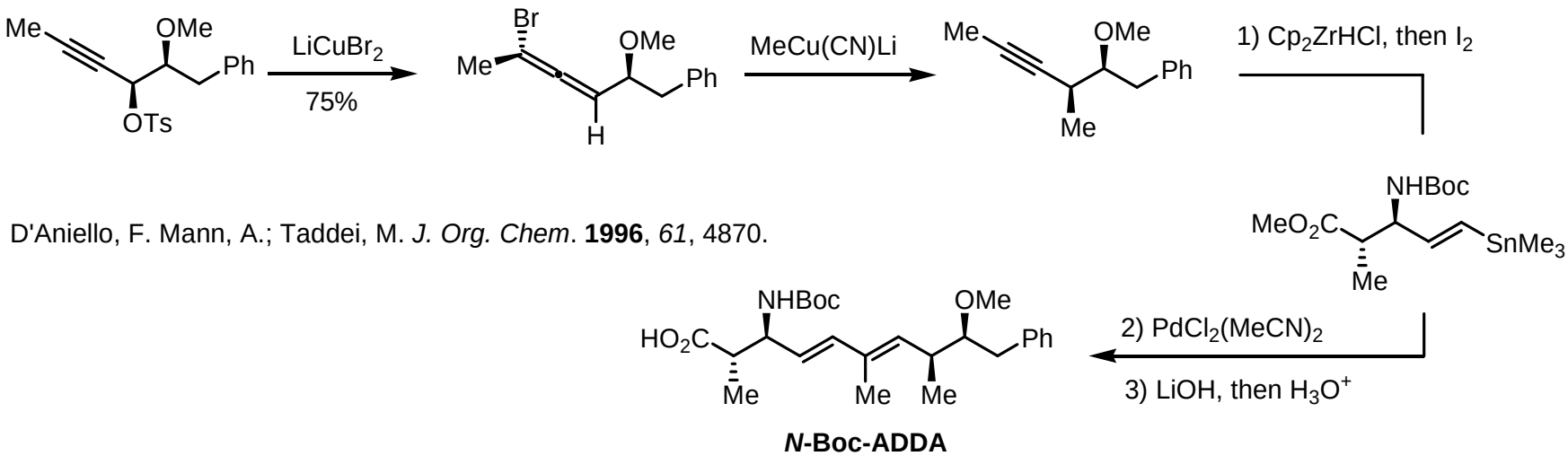

Buyanak, J. D. et al. *J. Am. Chem. Soc*. **1994**, *116*, 10955.

# $S_N2'$: C-X Bond Formation




Crimmins, M. T.; Emmitte, K. A.. *J. Am. Chem. Soc*. **2001**, *123*, 1533.

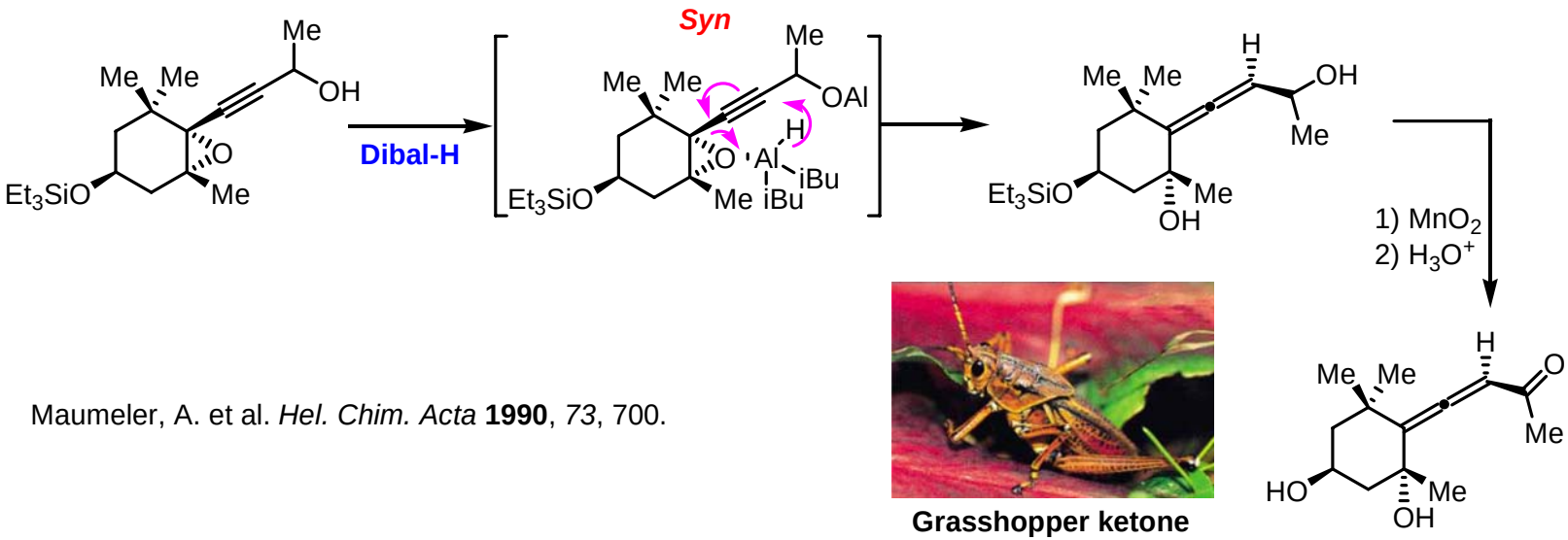
**(-)-Isolaurallene**



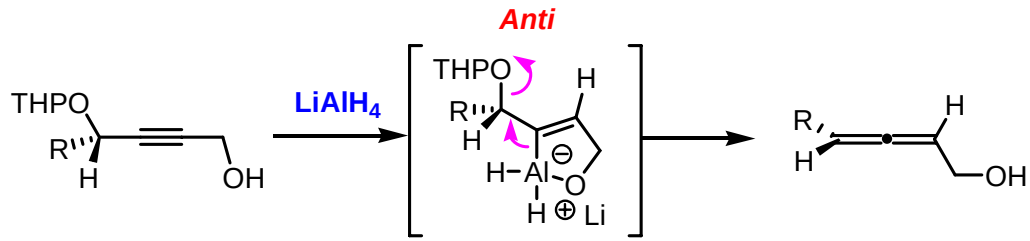

D'Aniello, F. Mann, A.; Taddei, M. *J. Org. Chem*. **1996**, *61*, 4870.

***N*-Boc-ADDA**

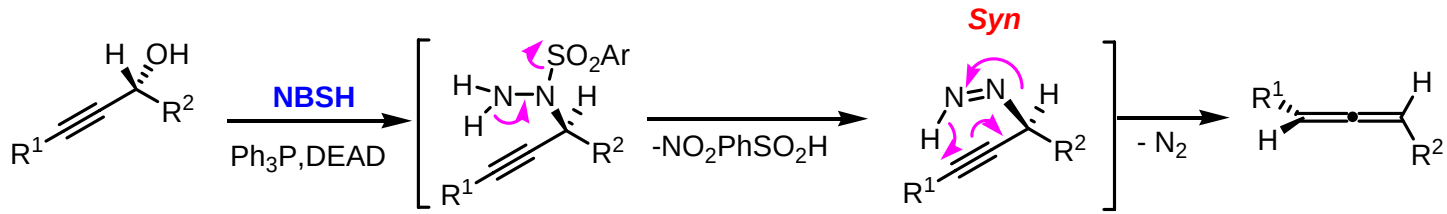
# $S_N2'$: C-H Bond Formation




Maumeler, A. et al. *Hel. Chim. Acta* **1990**, *73*, 700.

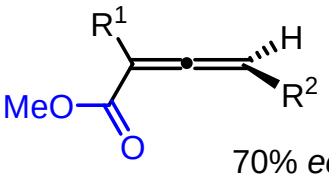



Berger, A. et al. *Synthesis* **1989**, 93.




Myers, A.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492.; Kitching, W. *J. Org. Chem*. **2003**, *68*, 3739.

# Pd Catalyzed Reactions

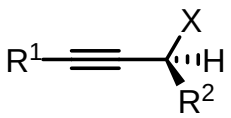



*J. Org. Chem.* **1997**, *62*, 367.

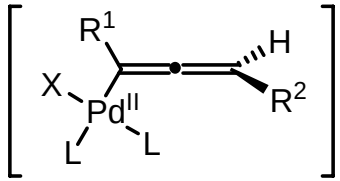
70% *ee* from 80% *ee*

CO (200 psi)
rt, MeOH/THF

X = OMs, $Pd_2(dba)_3$, $PPh_3$

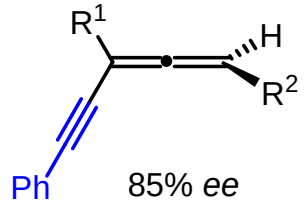



Pd(O)
***Anti***




Ph—≡—CuI

$ZnCl_2$, *i*$Pr_2NH$



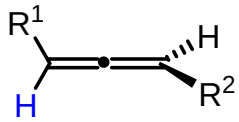

X = $OCO_2Me$, $Pd(PPh_3)_4$

85% *ee* from 93% *ee*

*Chem. Commun.* **1997**, 2083.

$LiEt_3BH$

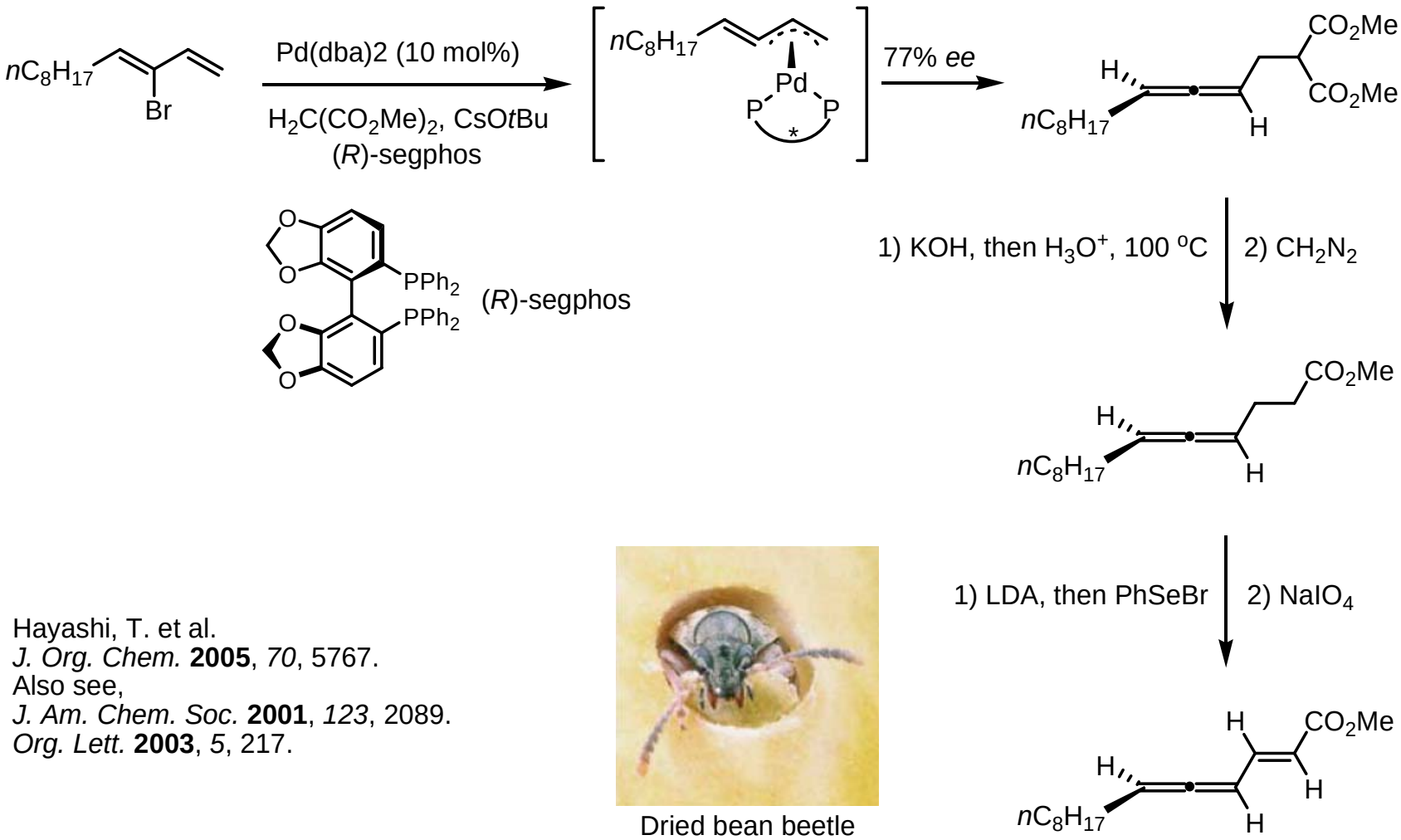
X = OMs, $Pd(PPh_3)_4$




*Tetrahedron Lett.* **1984**, *25*, 845.

49% *ee* from 58% *ee*

# Pd Catalyzed Allylic Substitution



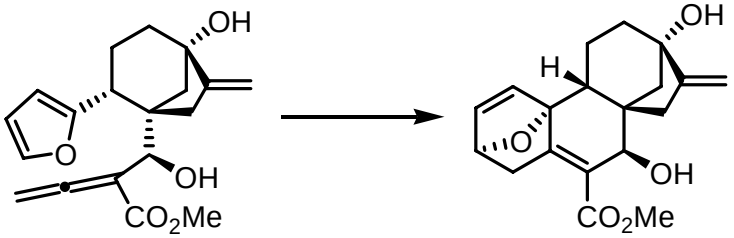

Hayashi, T. et al.
*J. Org. Chem.* **2005**, *70*, 5767.
Also see,
*J. Am. Chem. Soc.* **2001**, *123*, 2089.
*Org. Lett.* **2003**, *5*, 217.



Dried bean beetle

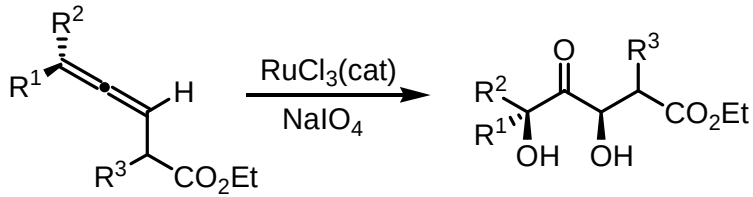
# Reactions of Allenes: General Survey

## Cycloaddition



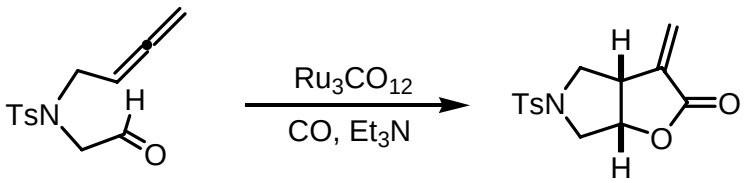

**A variety of [4+2], [3+3] cycloaddition reactions**

## Oxidation--Oxo transfer



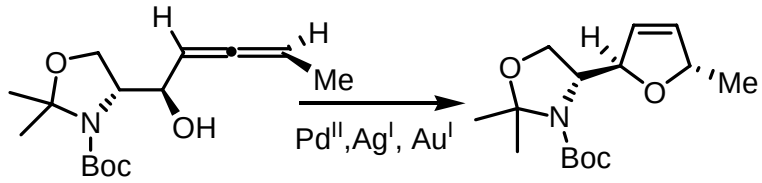

**Versatile substrate for oxidations**

## TM Catalyzed Addition to Allenes




**Various transition metal catalyzed cycloisomerization of allenes**

## Metal Mediated Ionic Reactions

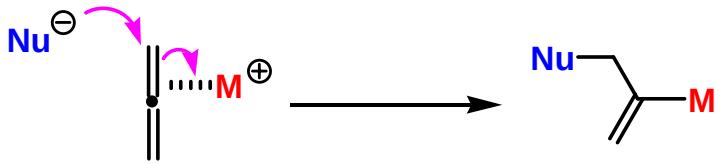



**As a unique substrate for many metallic cations**

Ma, S. *Chem. Rev.* **2005**, *105*, 2829-2871.

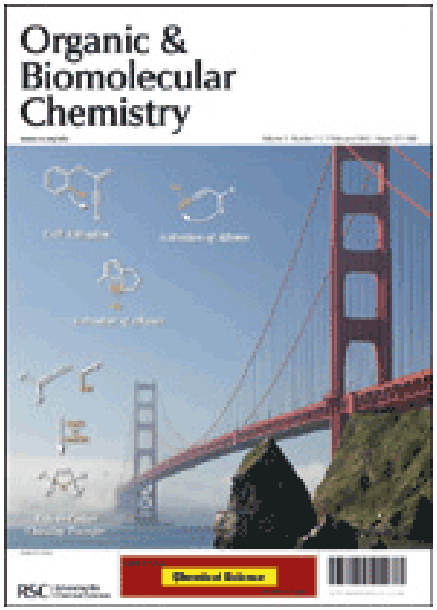
# Activating Metals for Allenes

Nu = O, N, C, S, X




M = **Pd, Ag, Au**

**Rh, Hg, Cu, Ce, Fp+, etc**



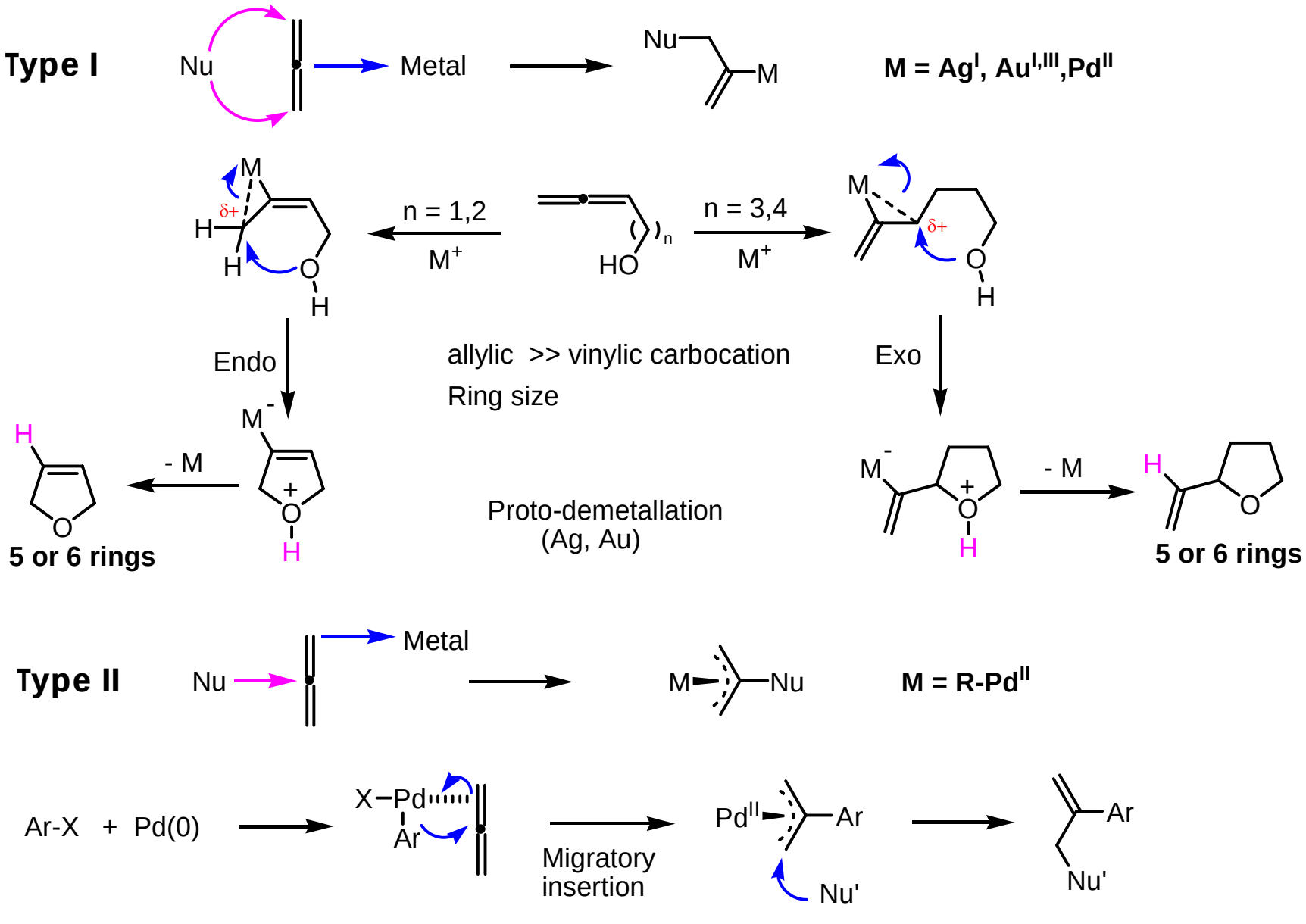

| | 10 | 11 |
|---|---|---|
| OS | II,IV | I |
| | **Pd** | **Ag** |
| EN | 2.20 | 1.93 |
| | II,IV | I,III |
| | **Pt** | **Au** |
| | 2.28 | 2.54 |

More electronegative...
more covalent character with C

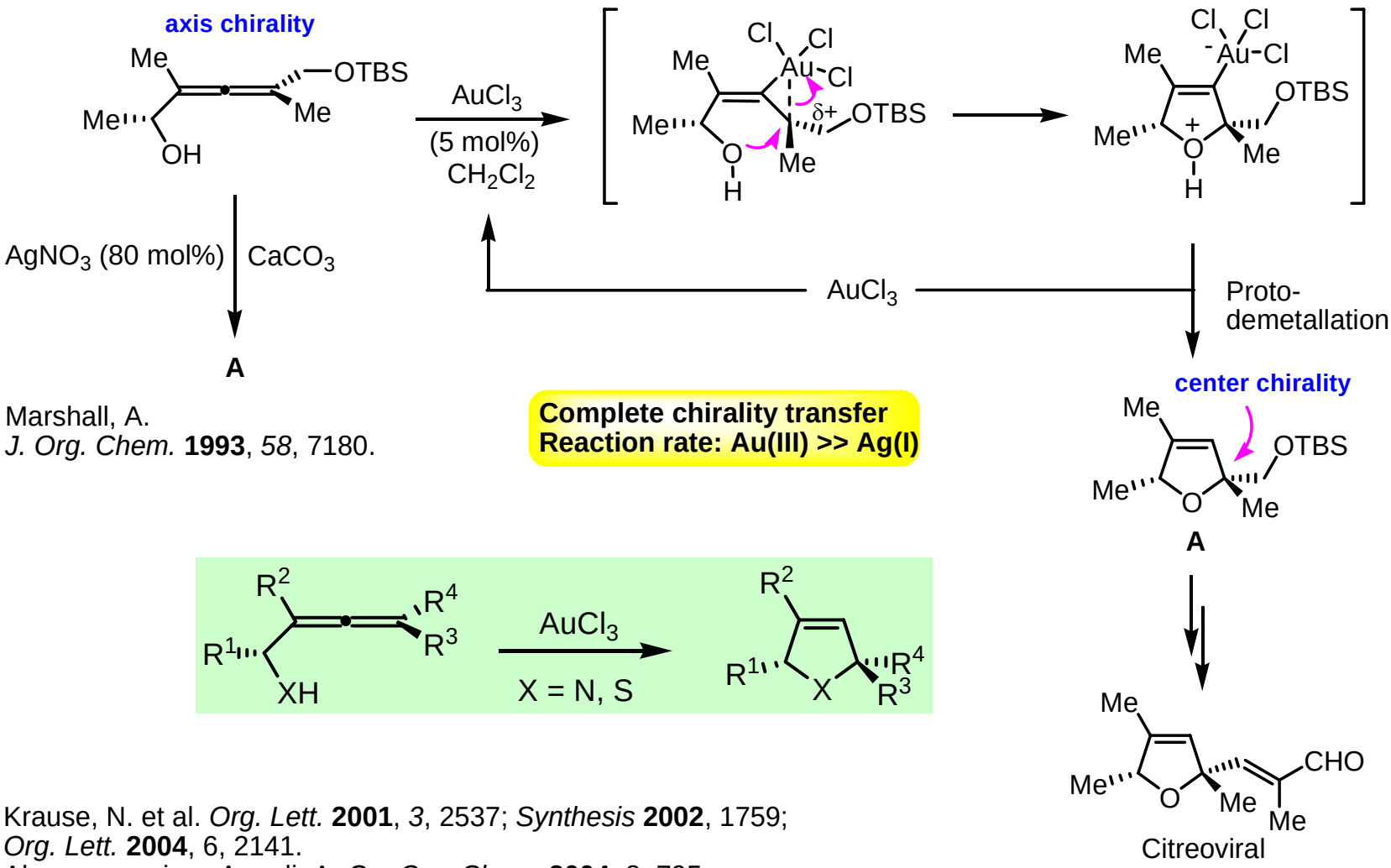
| | | |
|---|---|---|
| **Less** | Natural adundant | **More** |
| usually **II** | Oxidation State | Au **I, III** are capable of catalizing the same transformation |
| Re ⇄ Ox | Redox | Re ⇄ Ox (X) |
| **Yes** | β-H elimination | **No**, usually proto-demetallation--charateristic! |


Hoffmann-Roder, A.; Krause, N. "The Golden Gate to Catalysis" *Org. Biol. Chem.* **2005**, *3*, 387-391 and references cited therein.

# Regiochemical Courses



# Axis to Center Chirality Transfer



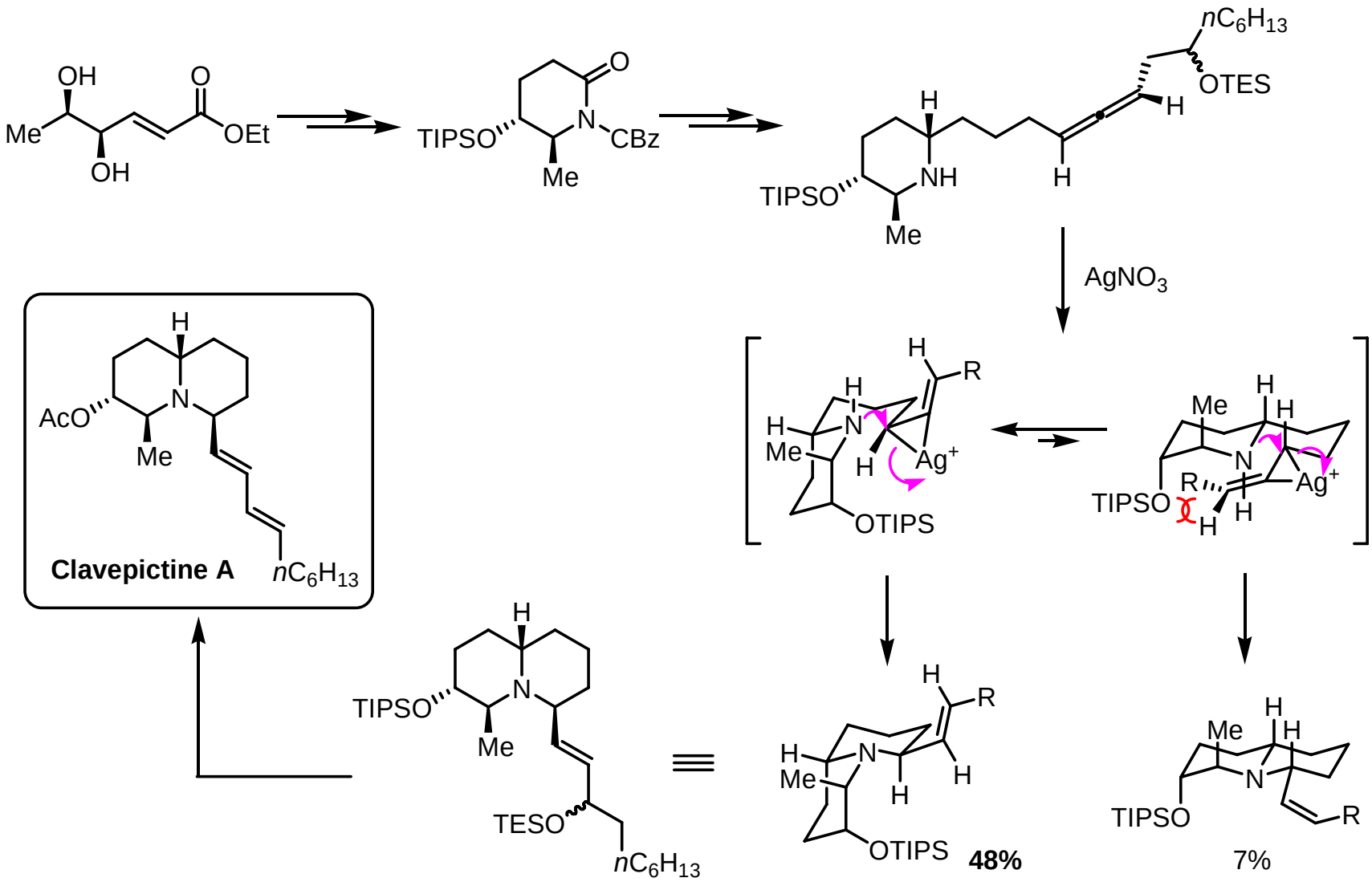

Marshall, A.
*J. Org. Chem.* **1993**, *58*, 7180.

**Complete chirality transfer**
**Reaction rate: Au(III) >> Ag(I)**



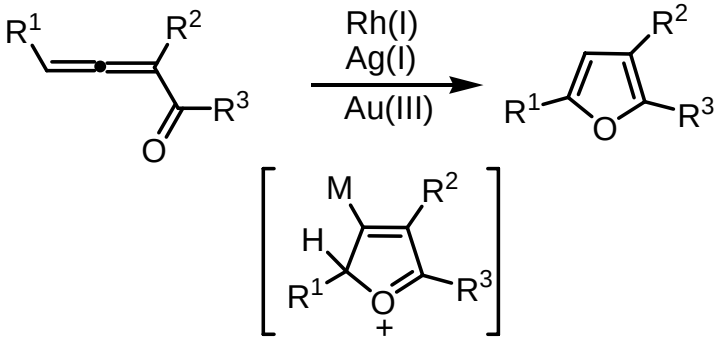

Krause, N. et al. *Org. Lett.* **2001**, *3*, 2537; *Synthesis* **2002**, 1759;
*Org. Lett.* **2004**, 6, 2141.
Also, see review: Arcadi, A. *Cur.Org. Chem.* **2004**, 8, 795.

# Exo case: Clavepictine A

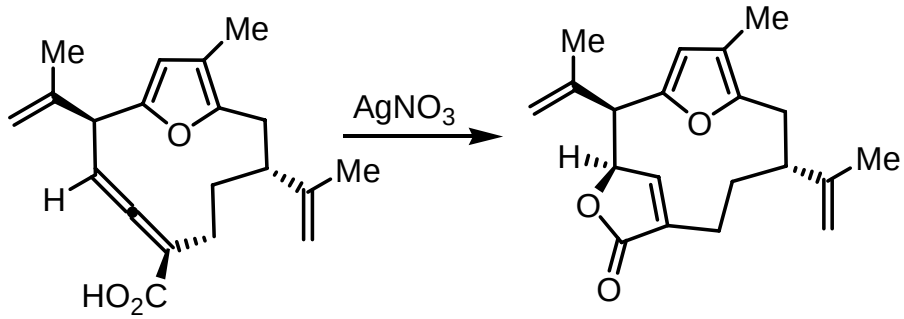



Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 10012.

# Allenyl ketones to Furan



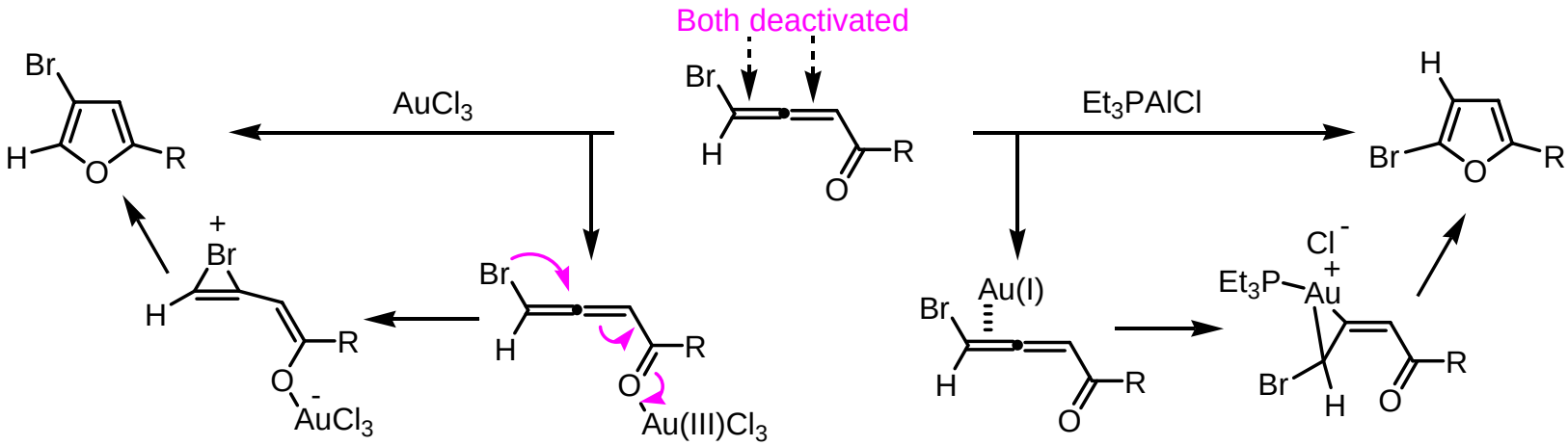

**Analogue (allenyl acid to furanone)**




Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 3450.
*J. Org. Chem.* **1995**, *60,* 3796.
Hashmi, A.S.K. *Angew. Chem. Int. Ed.* **2000**, *39*, 2285.

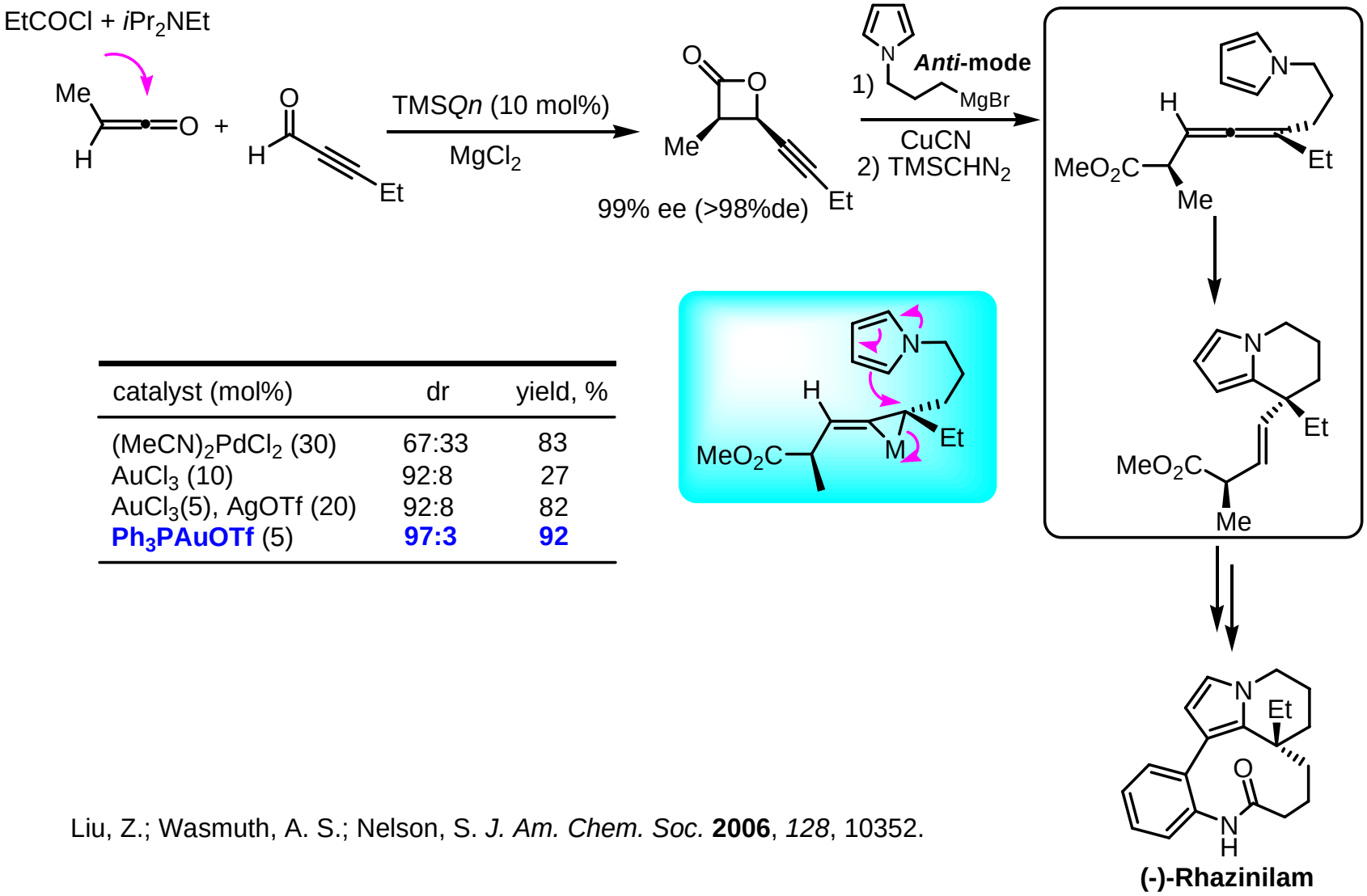
**Au(I) vs Au(III)**

Gevorgyan, V. et al. *J. Am. Chem. Soc.* **2005**, 127, 10500.




Highlight, Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2005**, *44*, 6990.

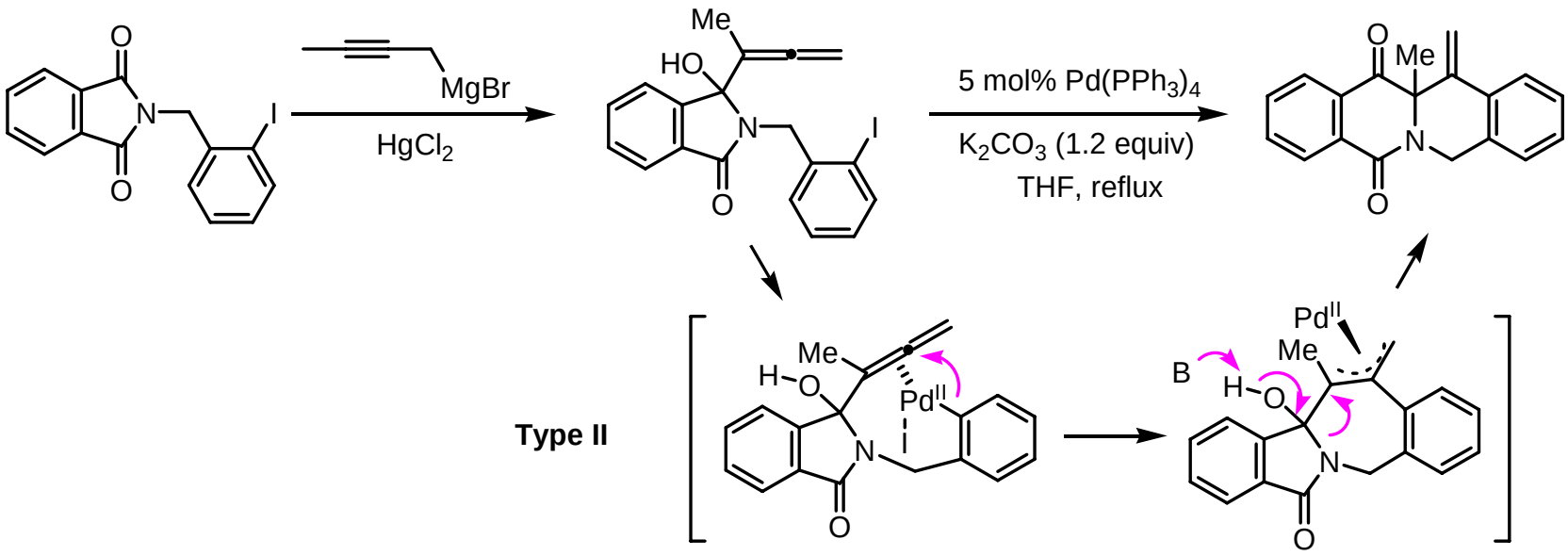
# C-C Bond Formation




| catalyst (mol%) | dr | yield, % |
|---|---|---|
| $(MeCN)_2PdCl_2$ (30) | 67:33 | 83 |
| $AuCl_3$ (10) | 92:8 | 27 |
| $AuCl_3$(5), AgOTf (20) | 92:8 | 82 |
| **$Ph_3PAuOTf$** (5) | **97:3** | **92** |

Liu, Z.; Wasmuth, A. S.; Nelson, S. *J. Am. Chem. Soc.* **2006**, *128*, 10352.

# Pd(II) Mediated Reactions

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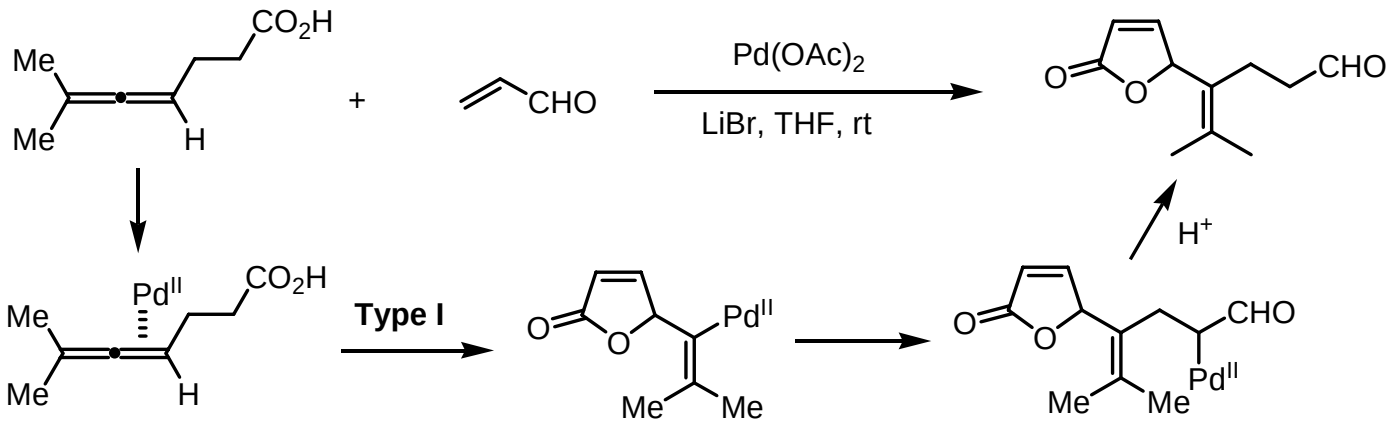


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# Summary

**Synthesis of allenes**: The most standard and convenient method for the asymmetric synthesis of allenes is the manipulation of chiral propargyl alcohol derivatives, for which recent progress of catalytic asymmetric synthetic methods would provide a wide variety of chiral starting materials.

**Reaction of allenes**: Allene, a very interesting compound with a hybrid character of an olefin and an acetylene, is a versatile functionality because it is useful as either a nucleophile or an electrophile and also as a substrate for many chemical transformations mediated metal catalysts. This multi-reactivity makes an allene as excellent candidate for many synthetic manipulations.

**Outlook**: Some recent reports have demonstrated the potential usefulness of axially chiral allenes as synthon. However, methods for supplying the optically pure allenes are still limited. Further novel asymmetric catalysis for the preparation of allenes will certainly be developed. Application of allenes in useful stereoselective synthesis has been made possible by the use of chiral allenes and exciting developments in this field in the near future seem certain.