

Useful articles:

Fairlamb, *ACIEE*, 2004, 1048.

Aubert et al., *Chem. Rev.*, 2002, 813.

Fletcher et al., *J. Chem. Soc., Perkin 1*, 2000, 1657.

Fürstner et al., *Chem. Eur. J.*, 2004, 4556.

Kozmin et al. *Adv. Synth. Catal.*, 2006, 2271.

Lloyd-Jones, *OBC*, 2003, 215.

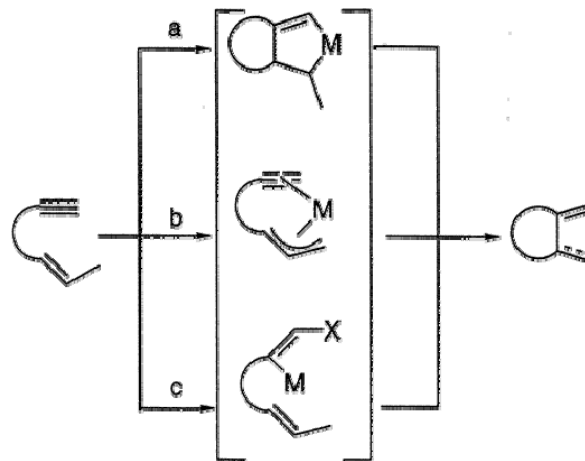
Toste et al., *Nature*, 2007, 395.

Ojima et al., *Chem Rev.*, 1996, 635.

Trost et al., *Acc. Chem. Res.*, 1990, 34.

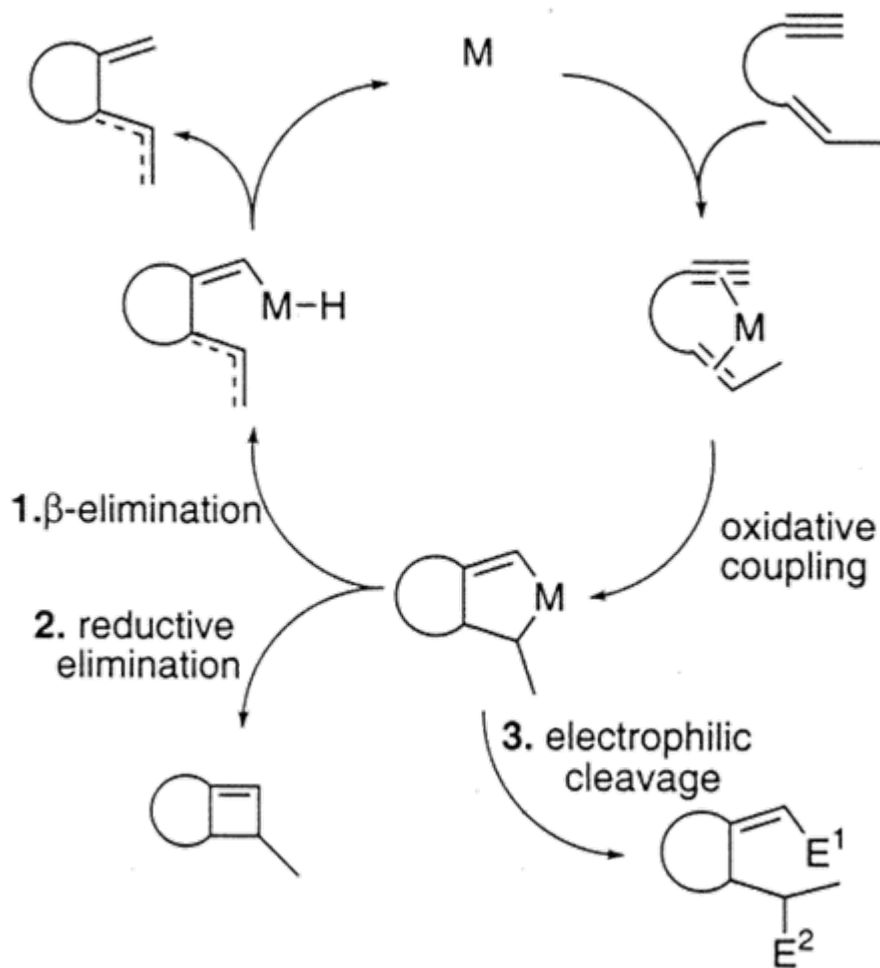
Trost et al., *Chem. Rev.*, 2001, 2067.

Trost et al., *Synlett*, 1998, 1.

Operating mechanisms:

- **A) The Metallo-cyclopentene Pathway**
 - β - elimination
 - Reductive elimination
 - Electrophilic cleavage
- **B) The π -Allylmetal Pathway**
- **C) The Vinylmetal Pathway**

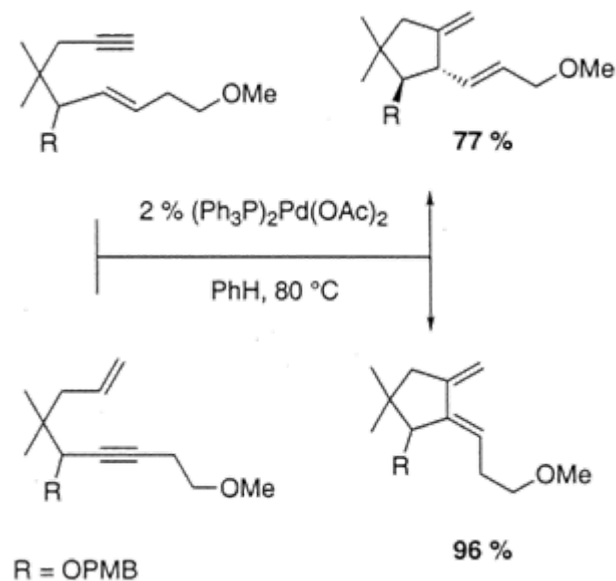
General mechanisms for enynes:



Aubert et al., Chem. Rev., 2002, 813.

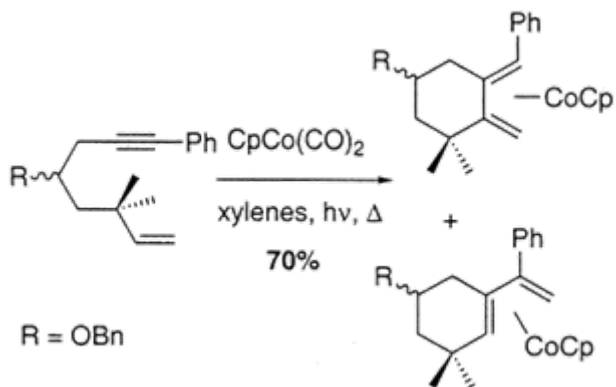
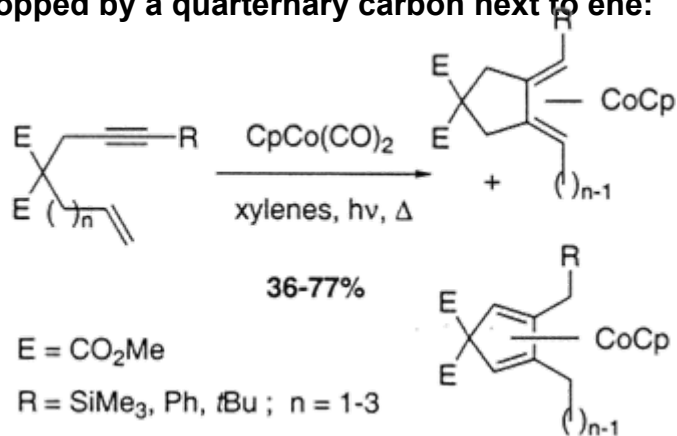
1. Metallopentene \rightarrow β -elimination

- Major and fastest pathway.
- Requires a vacant coordination site on the metal and cis relationship to eliminated proton.
- Generates 1,3- or 1,4-diene from enyne:
- Six metals usually applied: Pd, Ru, Rh, Co, Ir & Ti.
- Pd: 1,3-diene formed when allylic oxygen present and 1,4-diene formed when homoallylic oxygen present. Steric congestion favors 1,3-dienes.
- Interesting switch:



Trost et al., JACS, 1985, 1781; 1991, 636 & 1994, 4255.

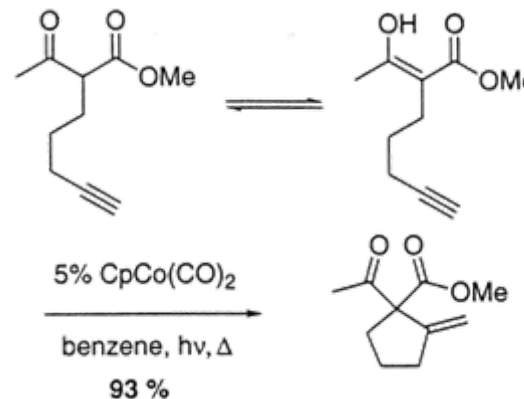
- Cobalt mediated a number of distinct cyclizations: Pauson-Khand, Intramolecular Nicholas reaction and cyclotrimerization.
- Enynes react with Co to form five-membered rings regardless of the length of the tether: This can be stopped by a quaternary carbon next to ene:



Fletcher et al., Perkin 1, **2000**, 1657.

Aubert et al., TetLett., **1996**, 7353 & Chem. Eur. J., **2001**, 3517.

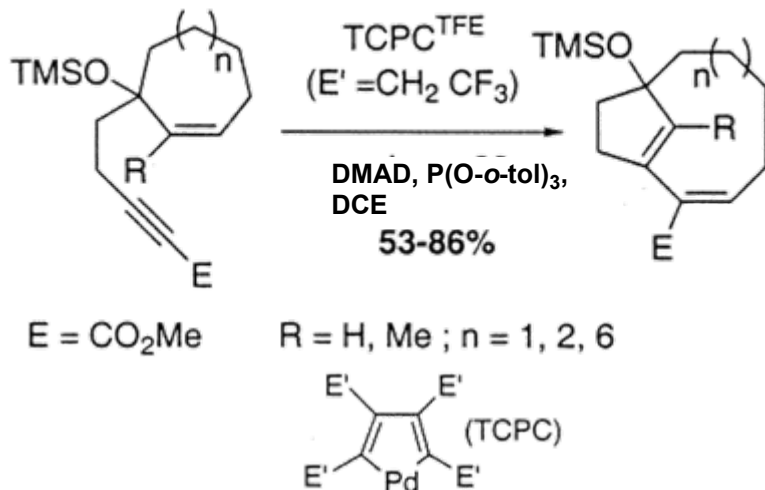
- Cobalt can also mediate a Conia ene-type reaction:



Stammler et al., Synlett, **1994**, 92.

2. Metallopentene -> Reductive-elimination

- When β-elimination is retarded reductive elimination becomes possible.
- The intermediate bicyclic cyclobutene of the formal [2+2] can be isolated, where thermal opening of cyclobutene isn't possible.
- Usually mediated by Pd, Pt or Ru.



- **EWG on the alkyne favors metaheis along with severe steric congestion.**

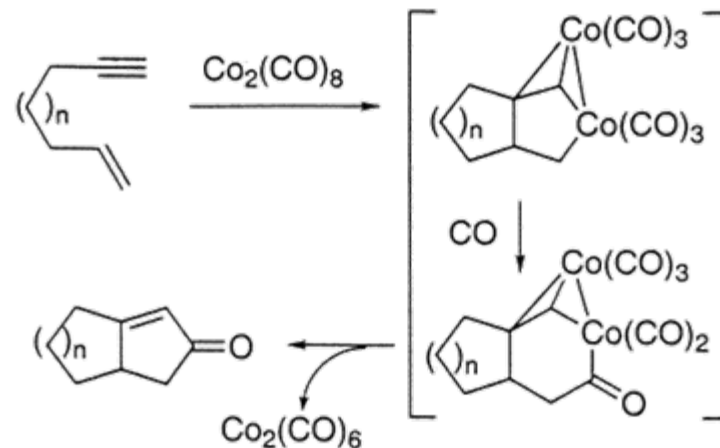
Trost & Trost, JACS, 1991, 1850.

- **Ruthenium carbene complexes are well known to mediate similiar reactions eg. olefin metathesis.**

3. Metallopentene -> Electrophilic cleavage

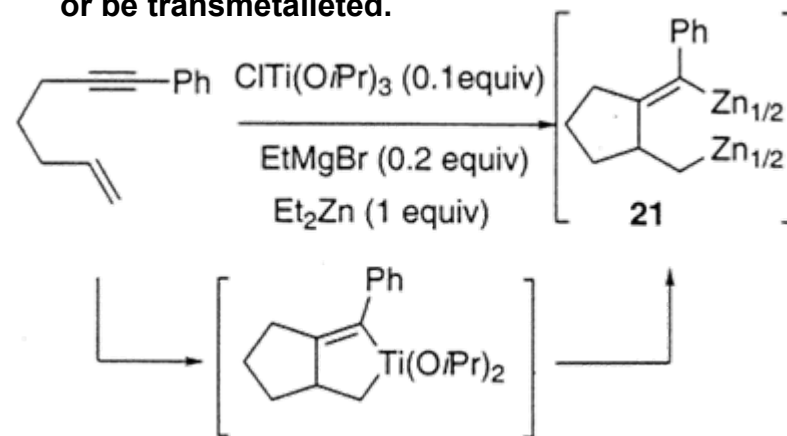
- **Occurs when no vacant coordination sites are present on the metal hence no β -elimination.**
- **Competes with reductive elimination with one or two electrophiles.**
- **Typically mediated by metals such as Ti, Co and Zr.**

The Pauson-Khand reaction

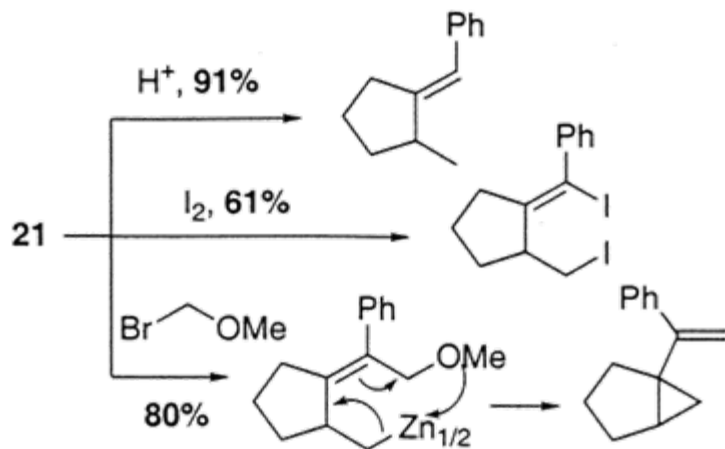


Khand, Pauson et al., Perkin 1, 1973, 977.

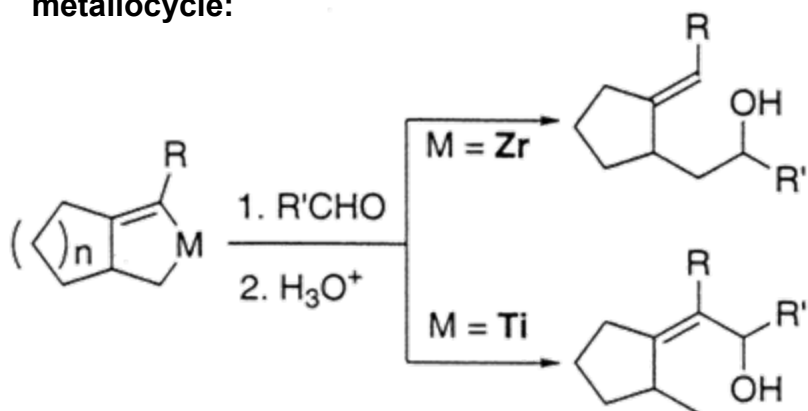
- **Reaction with different electrophiles: The metallopentene can react directly with electrophiles or be transmetalated.**



Negishi et al., JACS, 1998, 5345.



The two metal-carbon bonds can be differentiated with carbon electrophiles depending on the metallocycle:



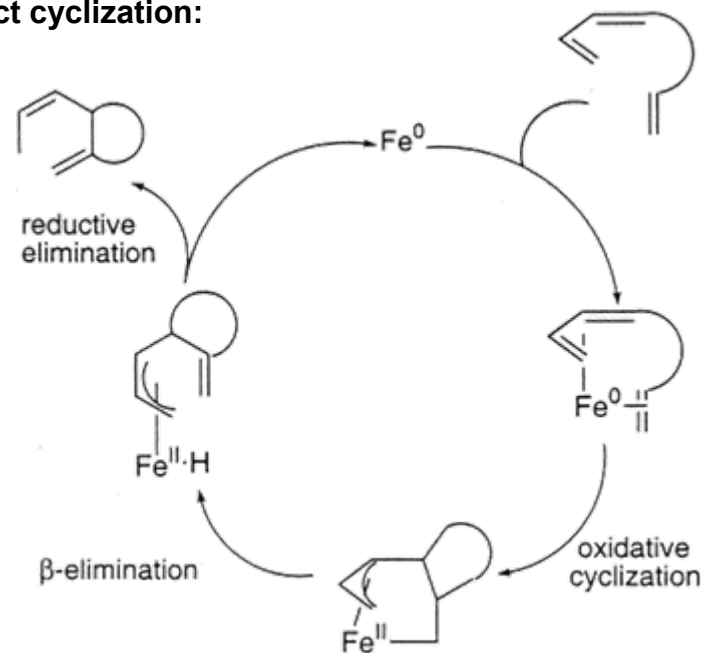
Hill et al., *Organometallics*, **1993**, 2911. Urabe et al., *JOC*, **1996**, 6756.

Negishi et al., *TetLett*, **1994**, 695.

The π -Allylmetal Pathway

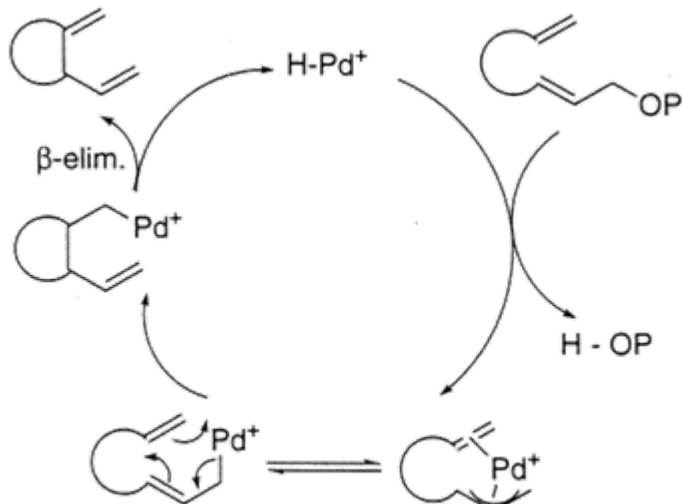
- Cyclization of enedienes generates a π -allylic complex with typically Fe or Pd.
- Pd can in addition react by preforming the π -allyl complex when a suitable leaving group is in the allylic position - known from the Tsuji-Trost reaction.

Direct cyclization:



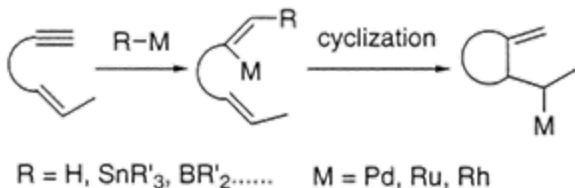
Takacs et al., *TetLett.*, **1990**, 2865; *TetLett.*, **1993**, 6219 & *JOC*; **1994**, 6928.

Cyclization after preformed allylmetal-complex:

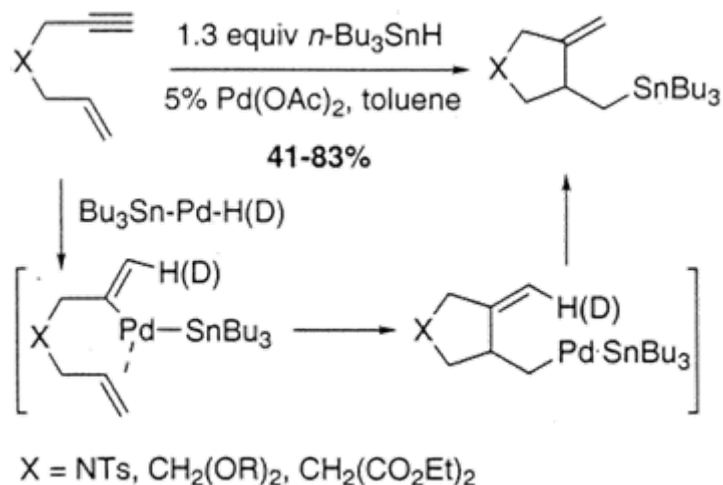


The Vinylmetal Pathway

- Addition of R-M-species across an alkyne leads to a vinylmetal intermediate capable of reacting with the alkene.
- M being Pd, Ru(enyne metathesis) and R being H, SnR'3 or BR'2.
- The vinylmetal can be generated from a carbon-halogen bond (Heck reaction)



- The cyclized intermediate can be intercepted or allowed to β-eliminate.
- Starting from tin-hydride the tin can be placed on the "other" branch.



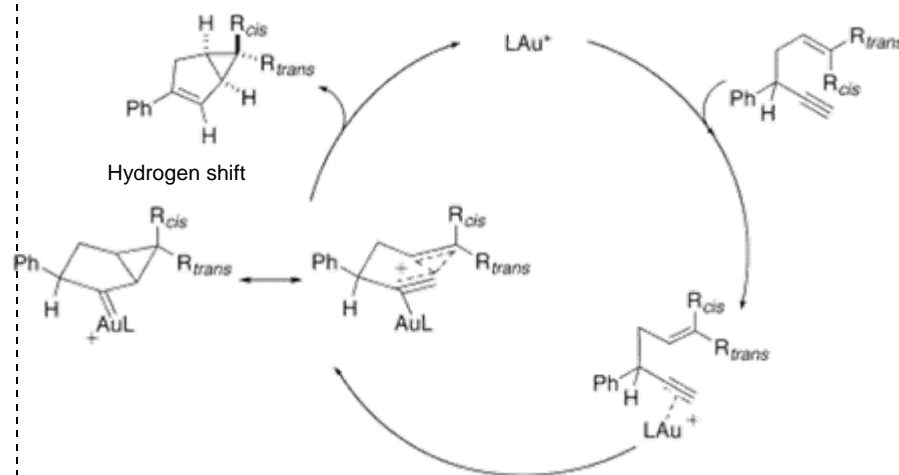
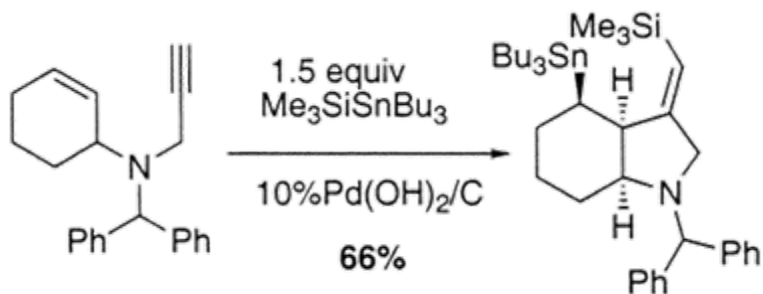
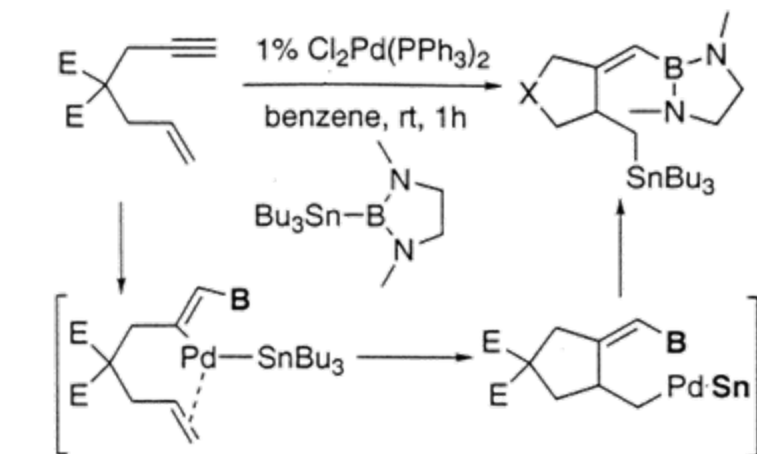
Trost et al., JACS, **1994**, 4268; TetLett., **1989**, 651.

Lautens et al., JOC, **2000**, 671.

Onozawa et al., Organometallics, **1997**, 5389.

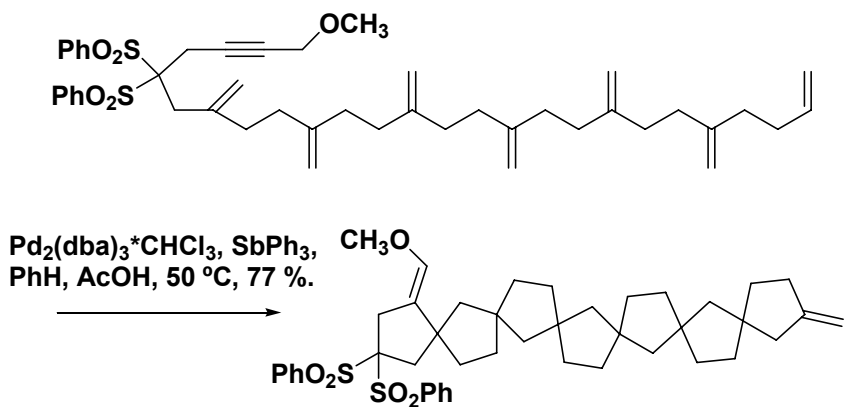
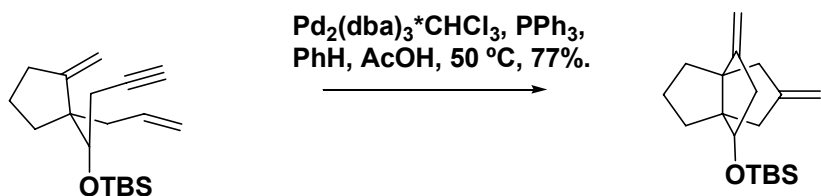
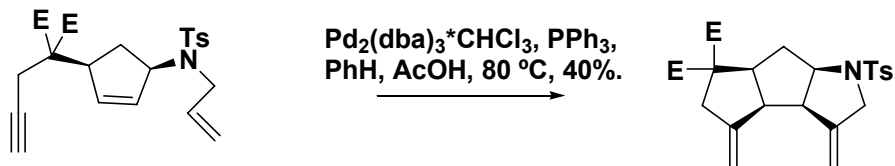
Mori et al., Organometallics, **2001**, 1907.

Gold(I) by another mechanism?

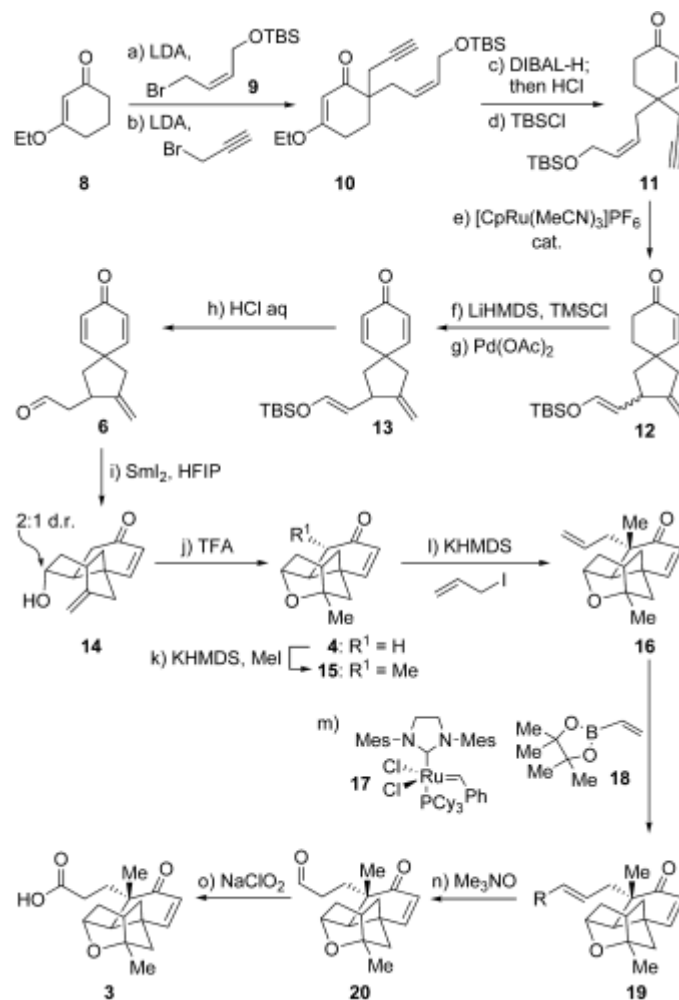


- Supported by deuterium-labelling and alkyl-shift.

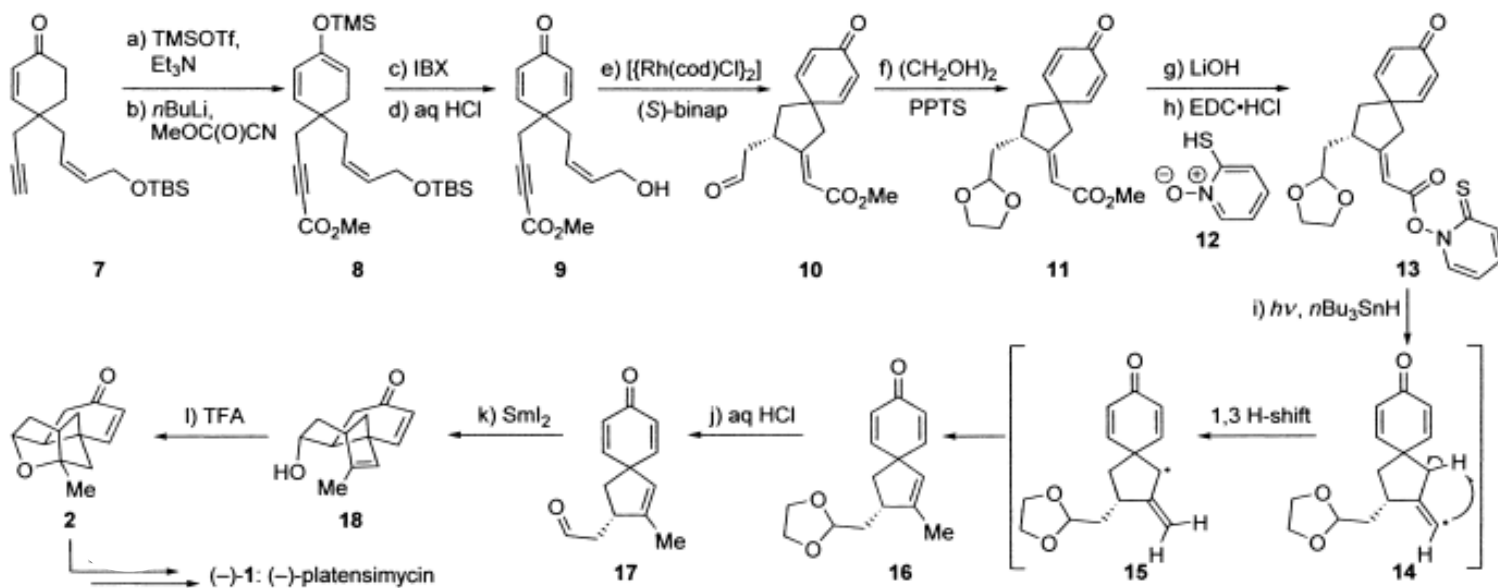
M. Luzung, J.P. Markham, F.D. Toste, JACS, 2004, 10858.

Application to synthesis:Trost et al., *Synlett*, **1998**, 1.Trost et al., *JACS*, **1993**, 9421.

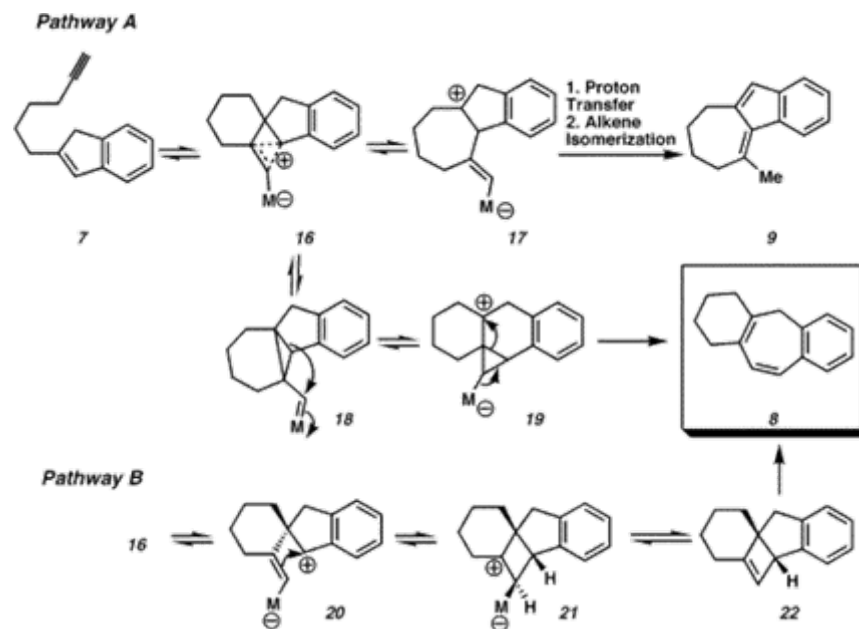
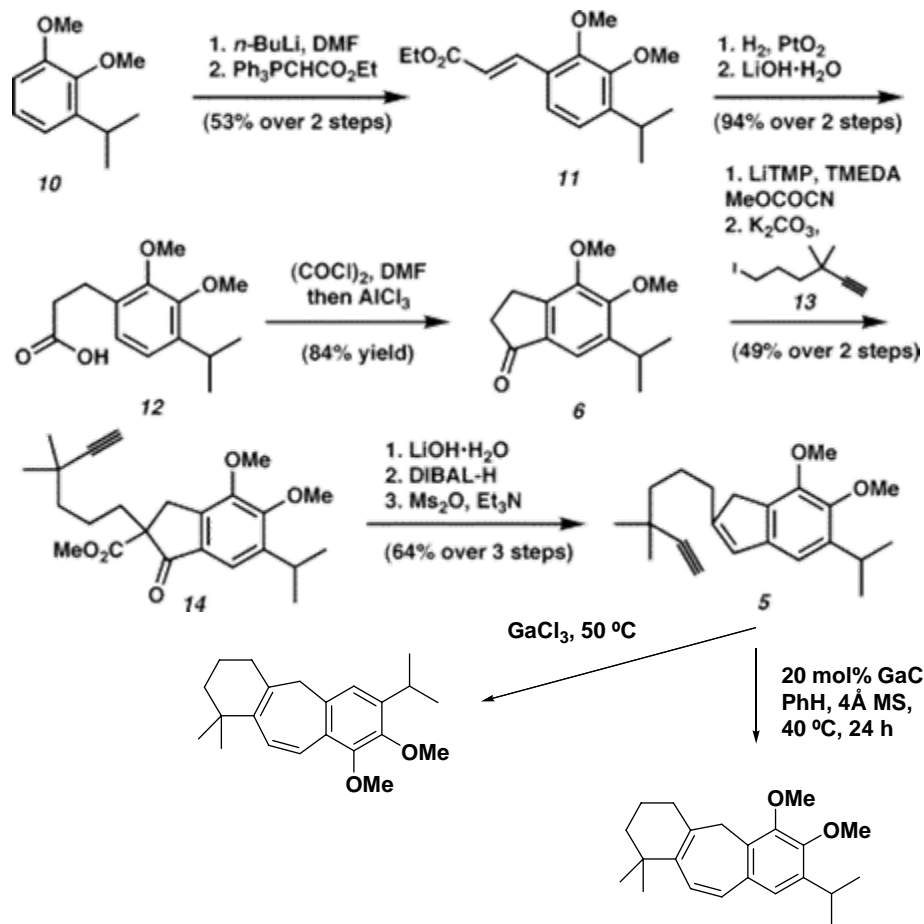
Total Synthesis of Platensimycin

K.C. Nicolaou, A. Li, E.J. Edmonds, *ACIEE*, **2006**, 7086

Asymmetric Total Syntheses of Platensimycin

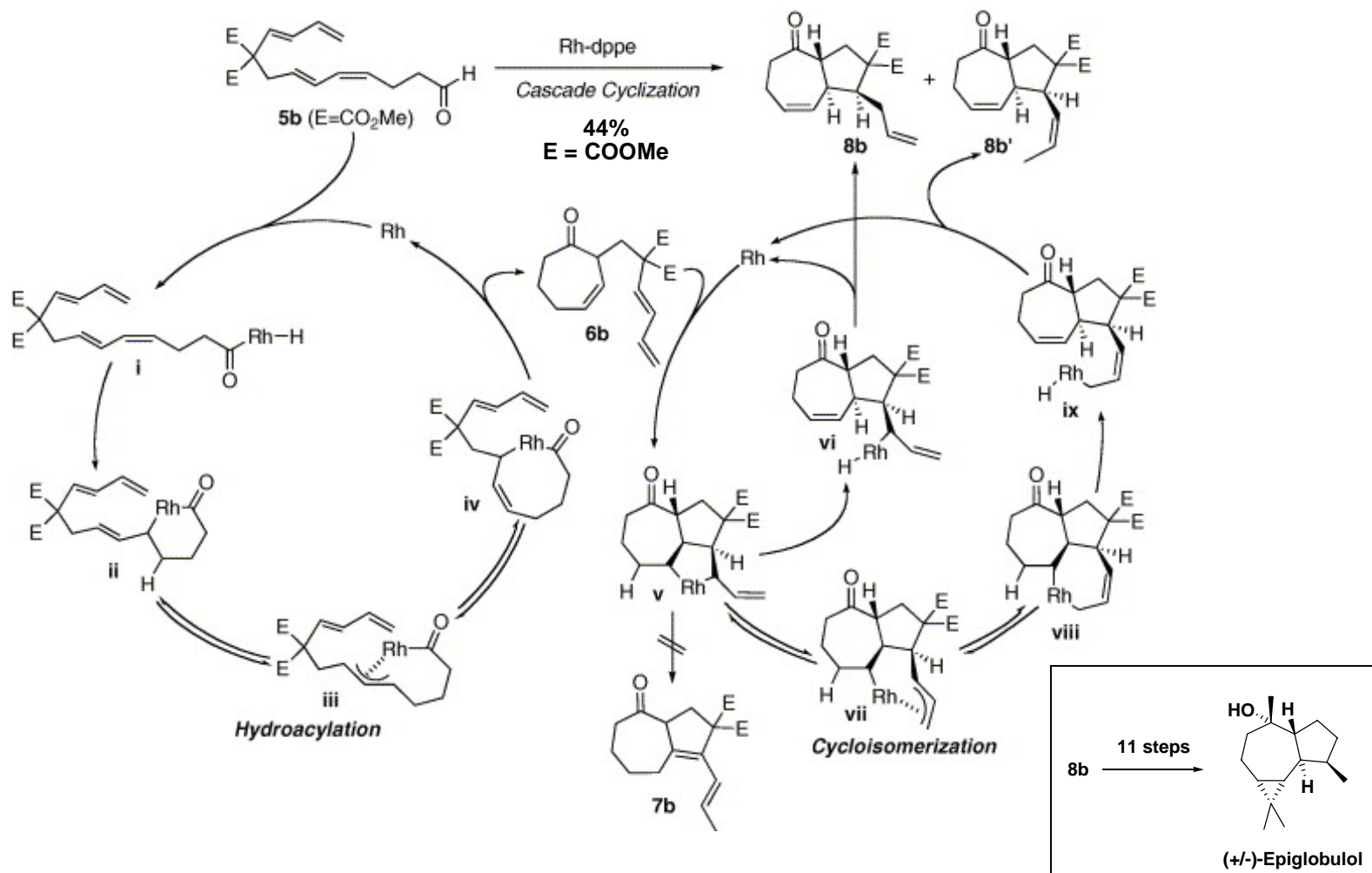
K.C. Nicolaou, E.J. Edmonds, A. Li, G.S. Tria, *ACIEE*, 2007, 3942

Total Synthesis of (+/-)-Salviasperanol

E.M. Simmons, R. Sarpong, *Org. Lett.*, 2006, 2883.

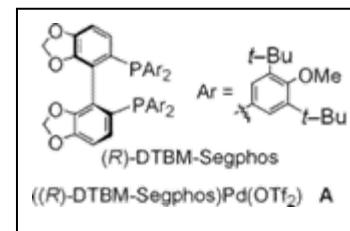
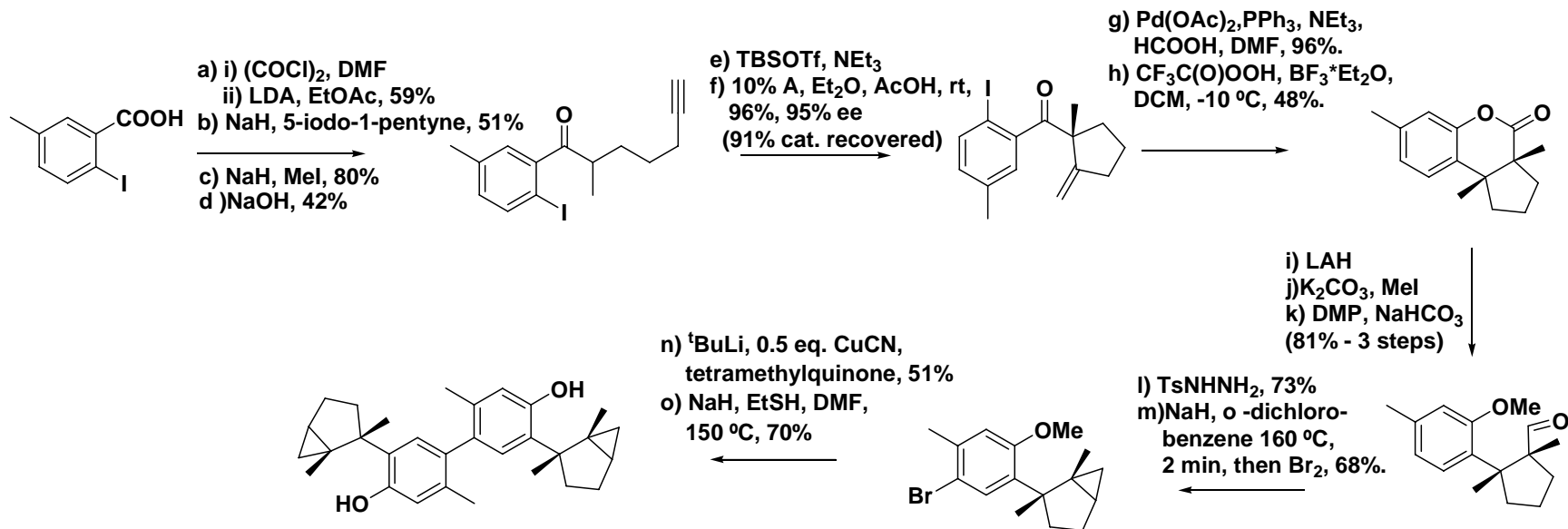
Synthesis of (+/-)-Epiglobulol

Y. Oonishi, A.Taniuchi, M. Mori, Y. Sato, Tet.Lett, 2006, 5617.



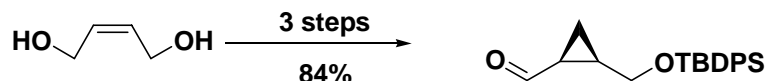
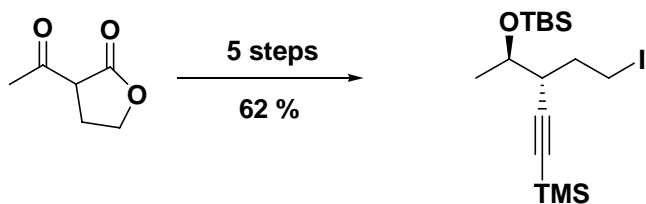
Total Synthesis of (-)-Laurebiphenyl

B.K. Corkey, F. D. Toste, JACS, 2007, 2764.

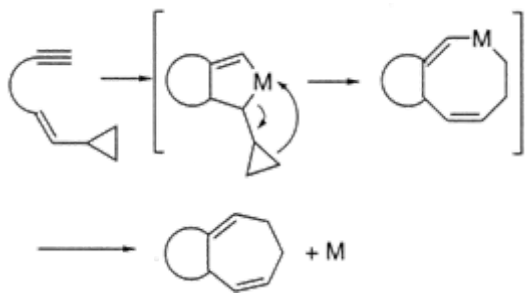


Total Synthesis of (-)-Pseudolaric Acid B

B.M. Trost, J. Waser, A. Meyer, JACS, 2007, 14556.

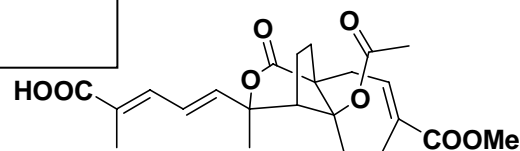
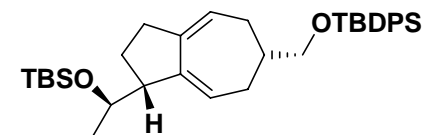
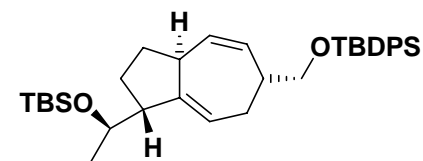
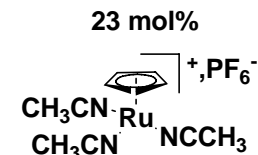
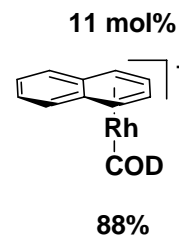
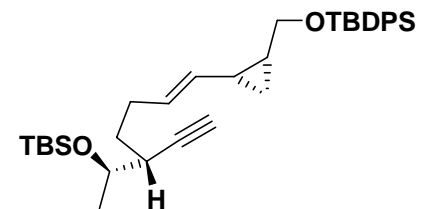


Mechanism:



i) Schlosser-wittig
olefination
ii) TMS-deprotection

58%, 53% E



Total Synthesis of the PicROTOXANE Sesquiterpenes

B.M. Trost, M.J. Krische, JACS, 1999, 6131 & 6183.

