

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.

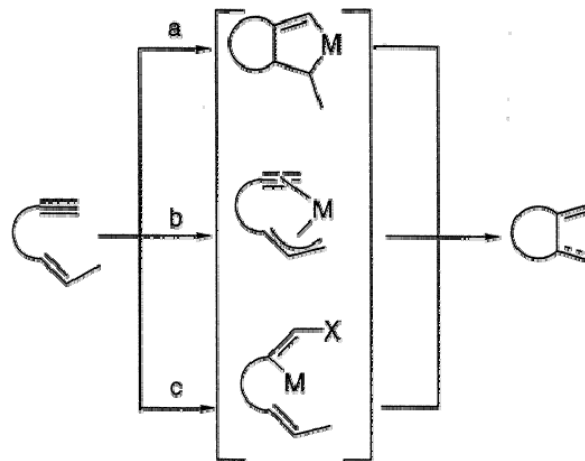
Toste et al., *Nature*, 2007, 395.

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

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

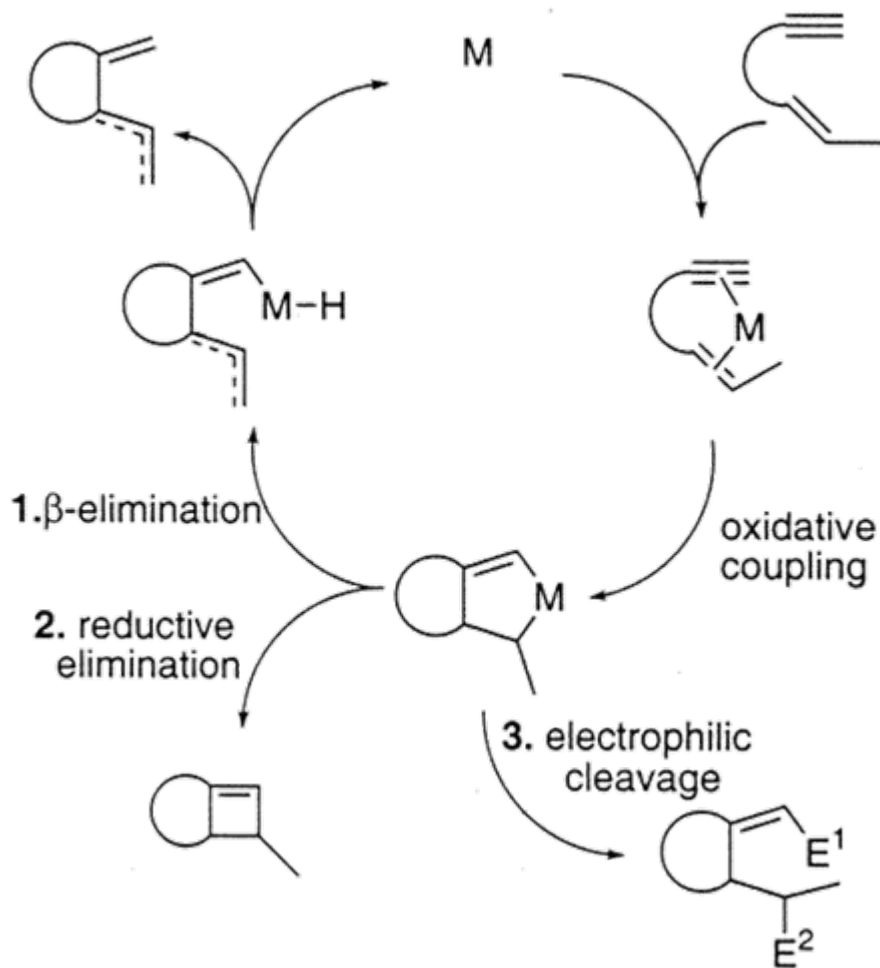
Trost et al., *Chem. Rev.*, 2001, 2067.

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

Operating mechanisms:

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

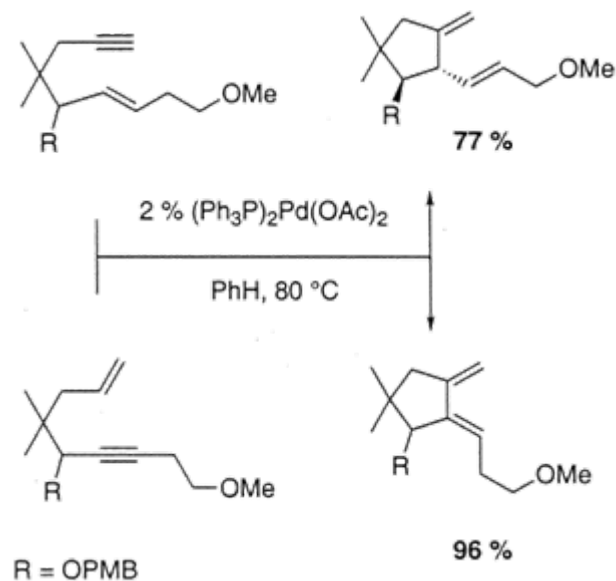
General mechanisms for enynes:



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

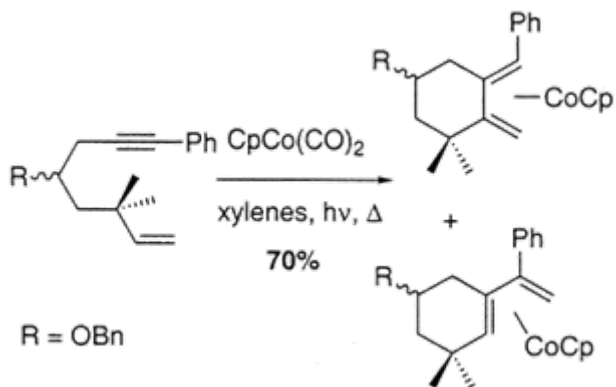
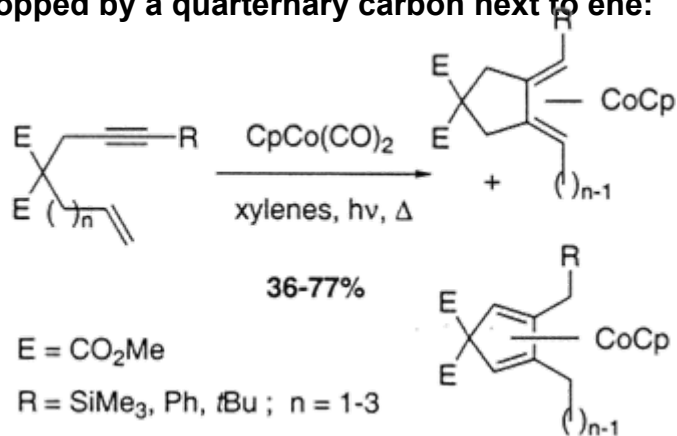
1. Metallopentene \rightarrow β -elimination

- 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.

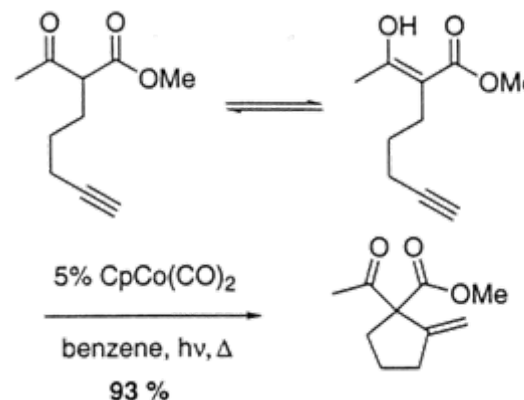
- Cobalt mediated a number of distinct cyclizations: Pauson-Khand, Intramolecular Nicholas reaction and cyclotrimerization.
- Enynes react with Co to form five-membered rings regardless of the length of the tether: This can be stopped by a quaternary carbon next to ene:



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

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

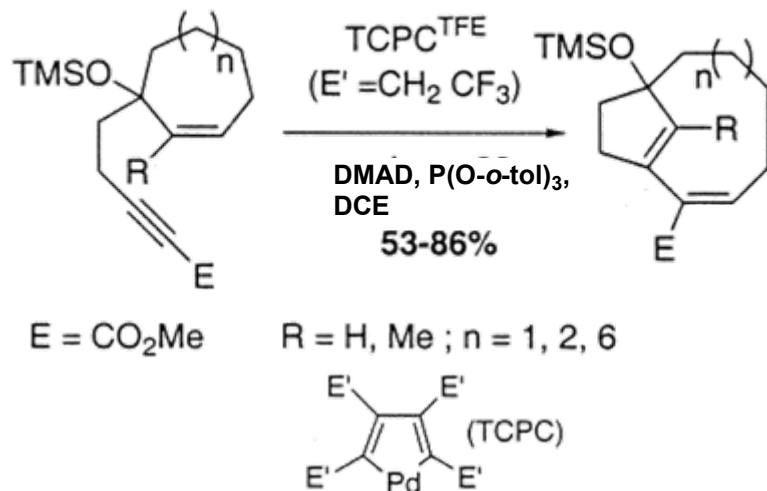
- Cobalt can also mediate a Conia ene-type reaction:



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.**

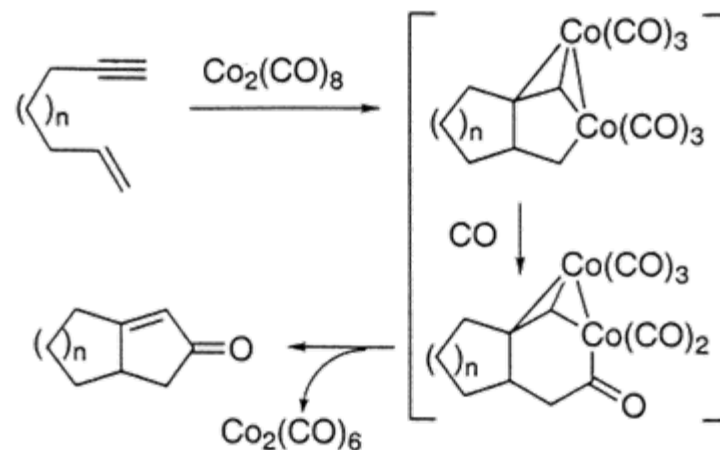
Trost & Trost, JACS, 1991, 1850.

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

3. Metallopentene -> Electrophilic cleavage

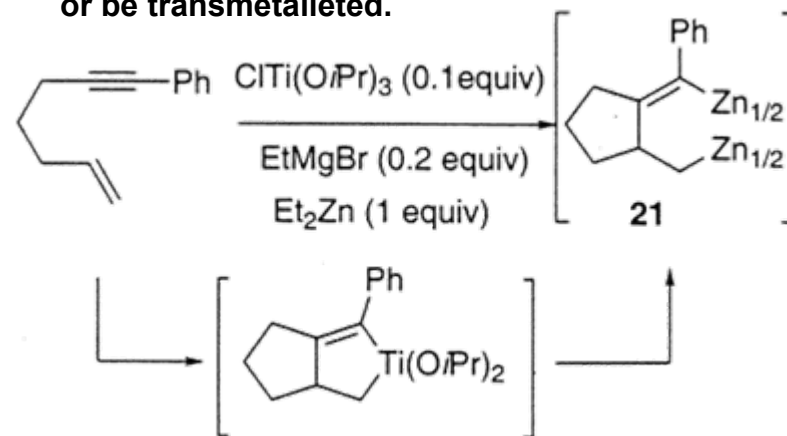
- **Occurs when no vacant coordination sites are present on the metal hence no β -elimination.**
- **Competes with reductive elimination with one or two electrophiles.**
- **Typically mediated by metals such as Ti, Co and Zr.**

The Pauson-Khand reaction

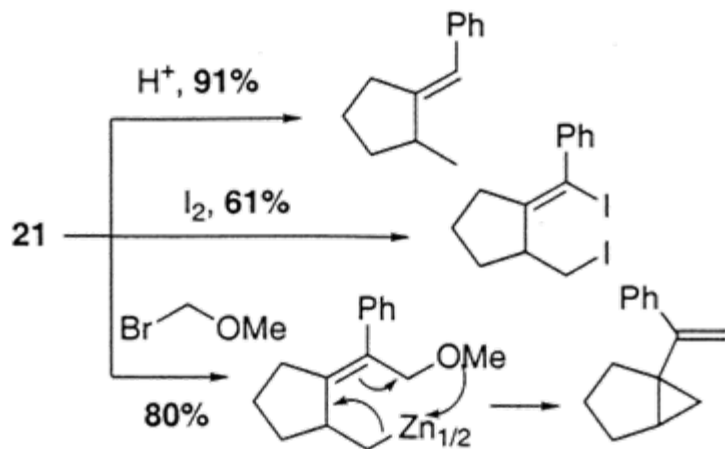


Khand, Pauson et al., Perkin 1, 1973, 977.

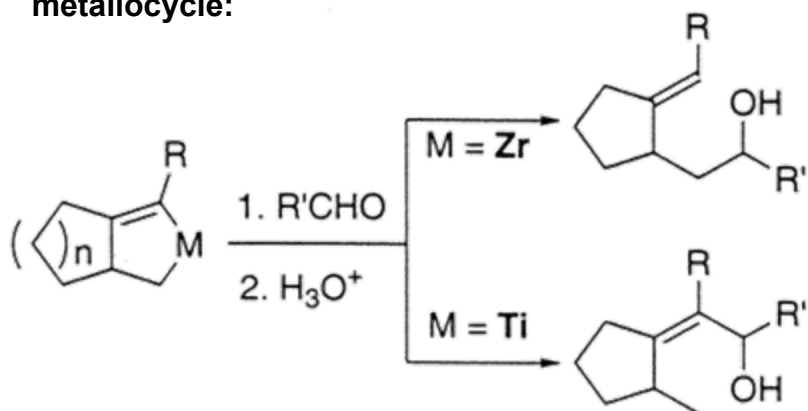
- **Reaction with different electrophiles: The metallopentene can react directly with electrophiles or be transmetalated.**



Negishi et al., JACS, 1998, 5345.



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



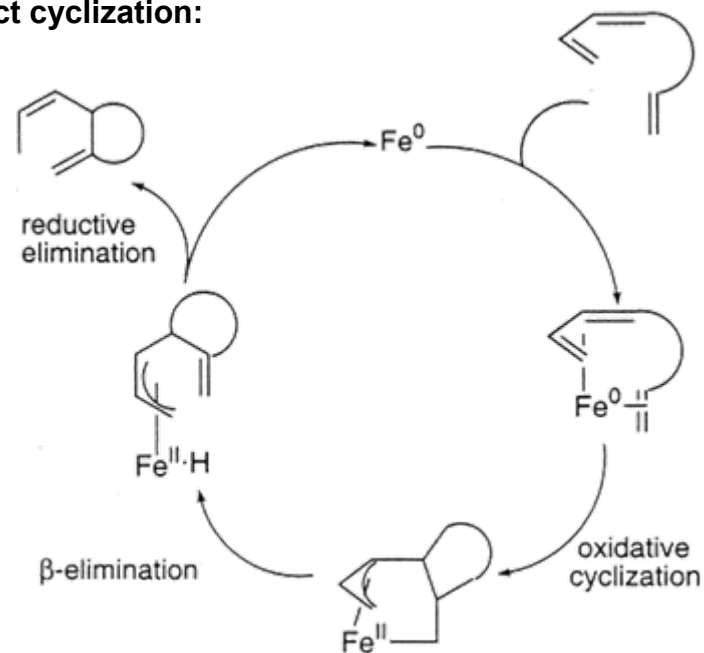
Hill et al., *Organometallics*, **1993**, 2911. Urabe et al., *JOC*, **1996**, 6756.

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

The π -Allylmetal Pathway

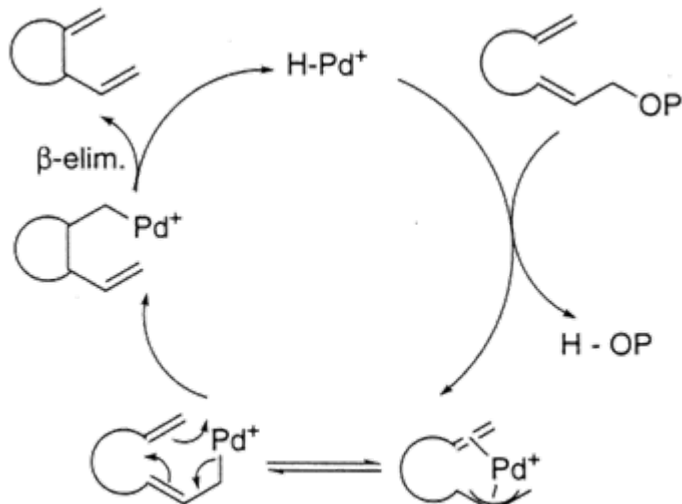
- Cyclization of enedienes generates a π -allylic complex with typically Fe or Pd.
- Pd can in addition react by preforming the π -allyl complex when a suitable leaving group is in the allylic position - known from the Tsuji-Trost reaction.

Direct cyclization:



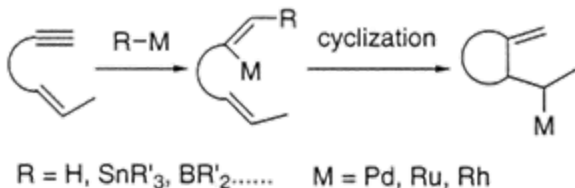
Takacs et al., *TetLett.*, **1990**, 2865; *TetLett.*, **1993**, 6219 & *JOC*; **1994**, 6928.

Cyclization after preformed allylmetal-complex:

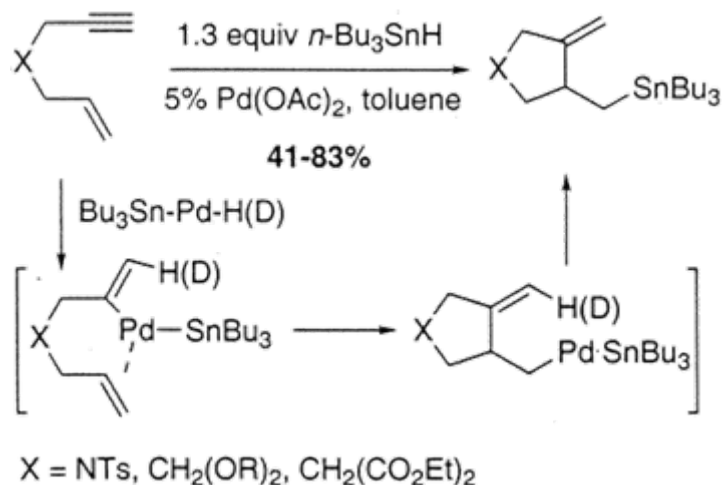


The Vinylmetal Pathway

- 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.



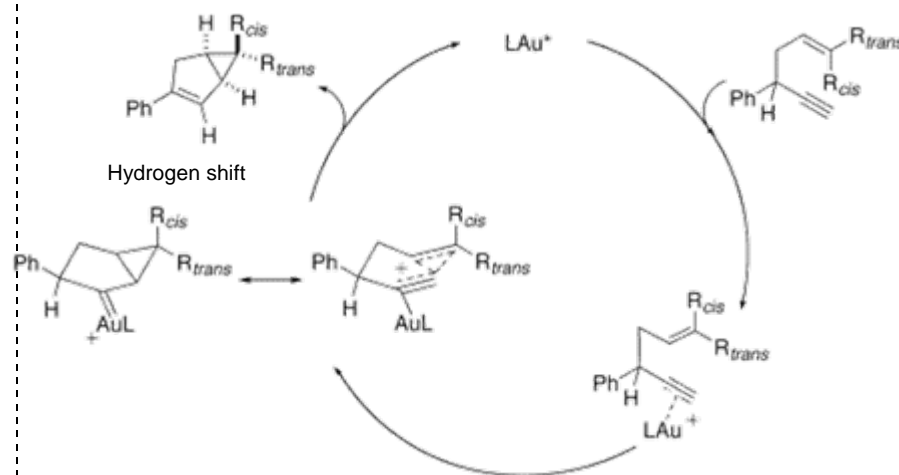
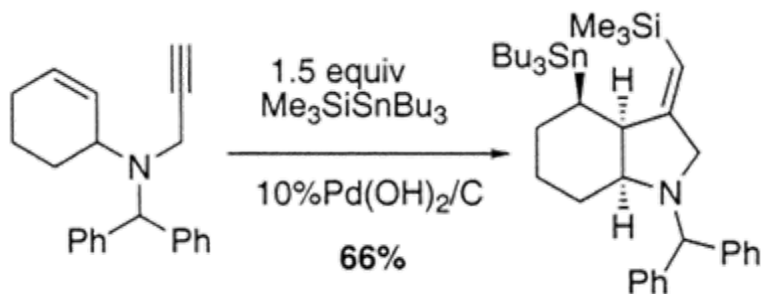
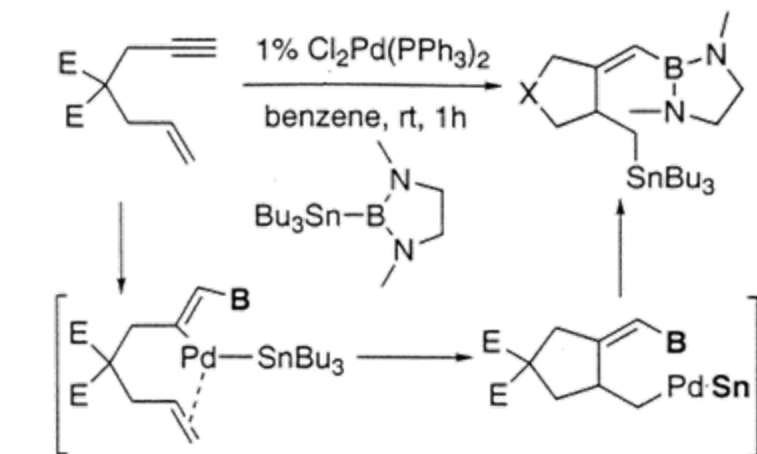
Trost et al., JACS, **1994**, 4268; TetLett., **1989**, 651.

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

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

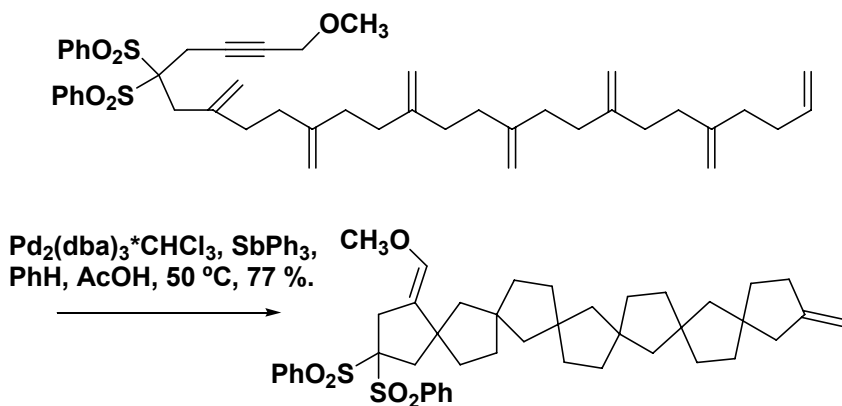
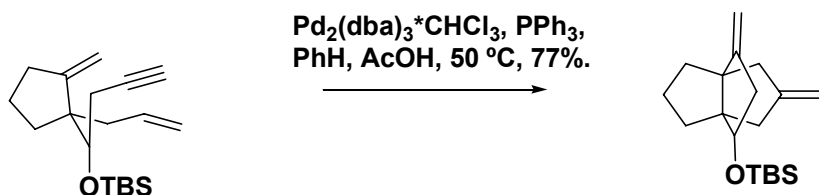
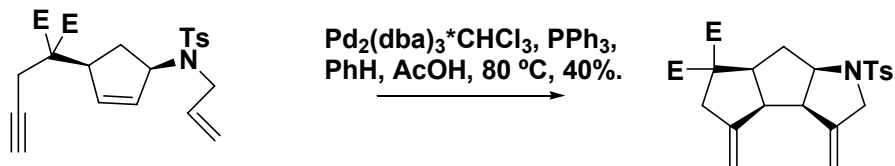
Mori et al., Organometallics, **2001**, 1907.

Gold(I) by another mechanism?



- Supported by deuterium-labelling and alkyl-shift.

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

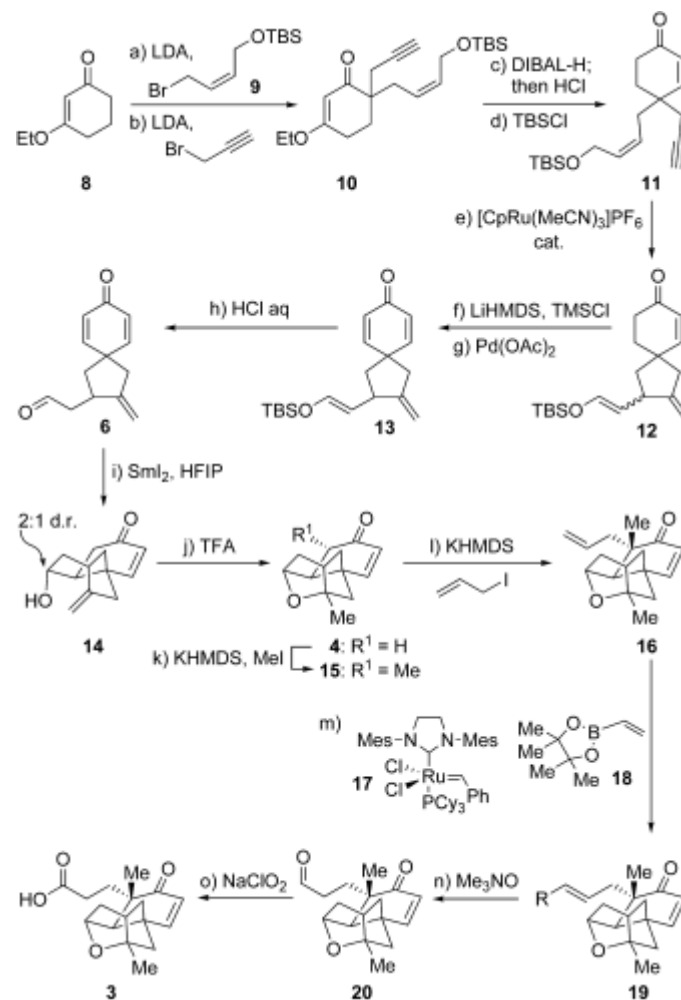
Application to synthesis:

Trost et al., Synlett, 1998, 1.

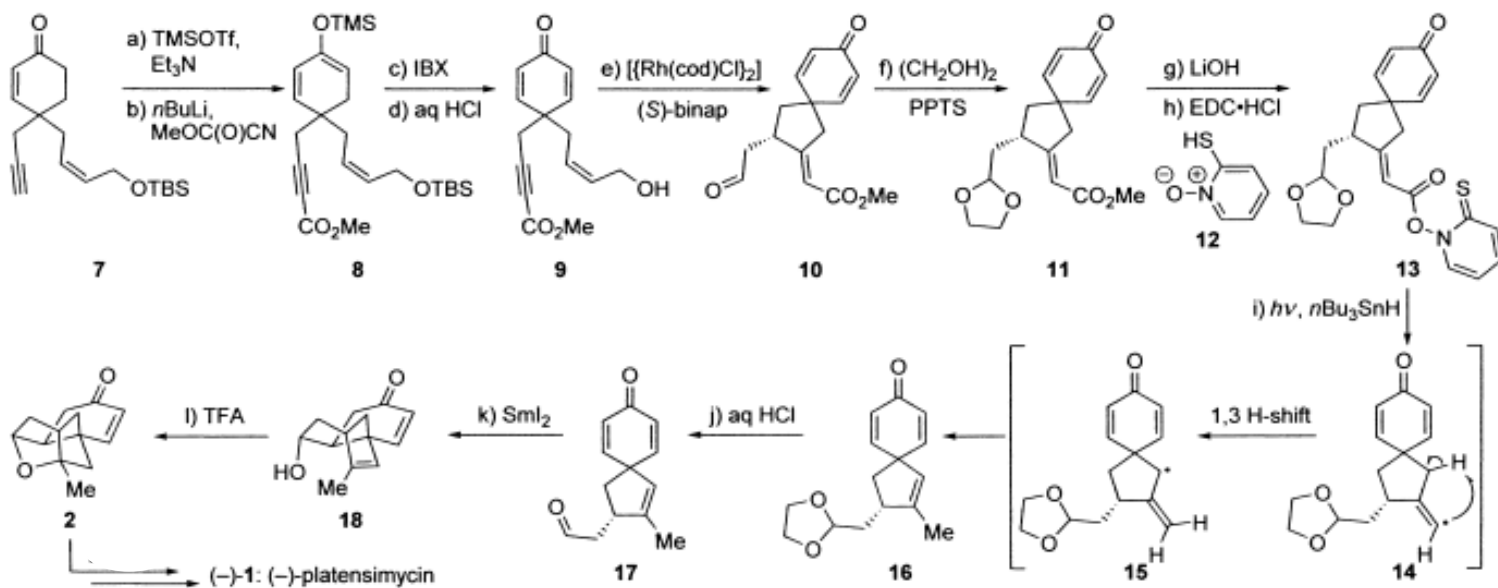
Trost et al., JACS, 1993, 9421.

Total Synthesis of Platensimycin

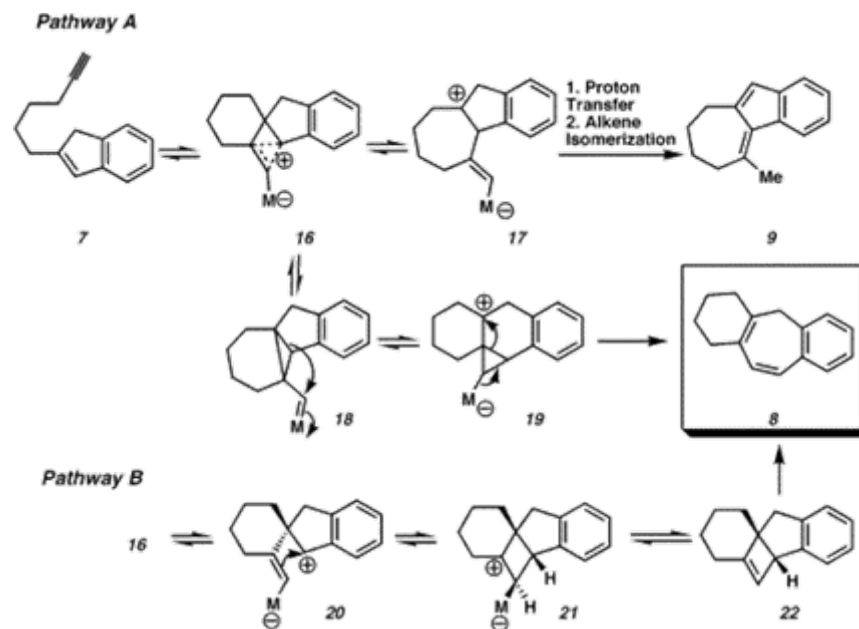
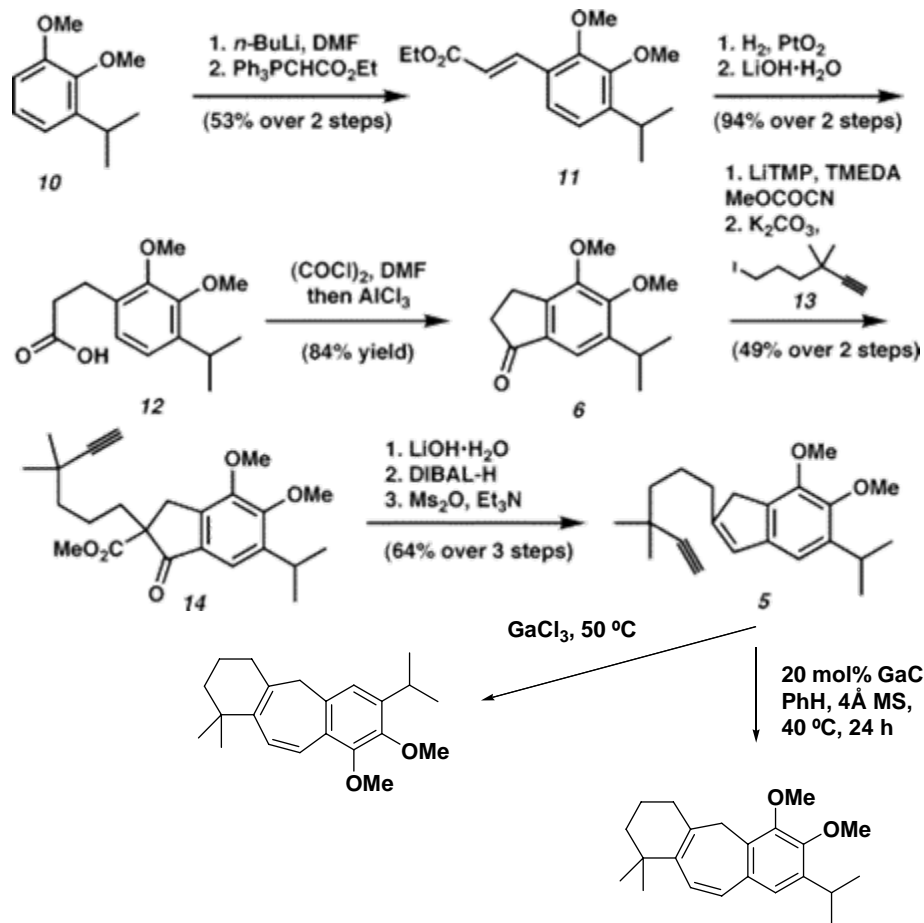
K.C. Nicolaou, A. Li, E.J. Edmonds, ACIEE, 2006, 7086



Asymmetric Total Syntheses of Platensimycin

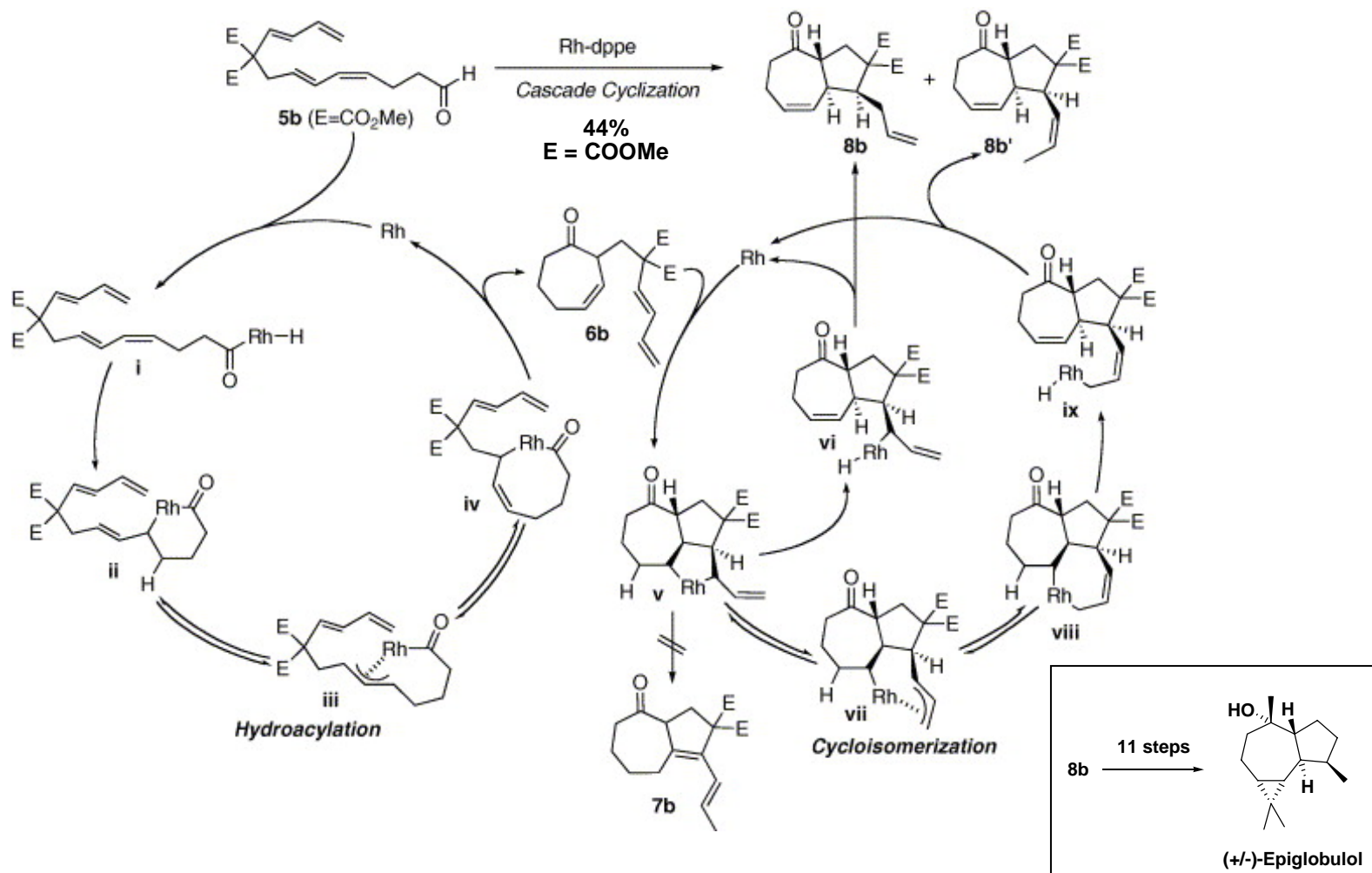
K.C. Nicolaou, E.J. Edmonds, A. Li, G.S. Tria, *ACIEE*, 2007, 3942

Total Synthesis of (+/-)-Salviasperanol

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

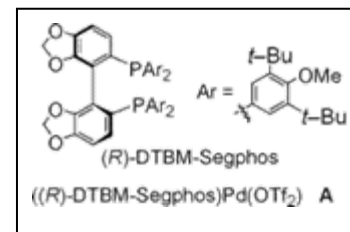
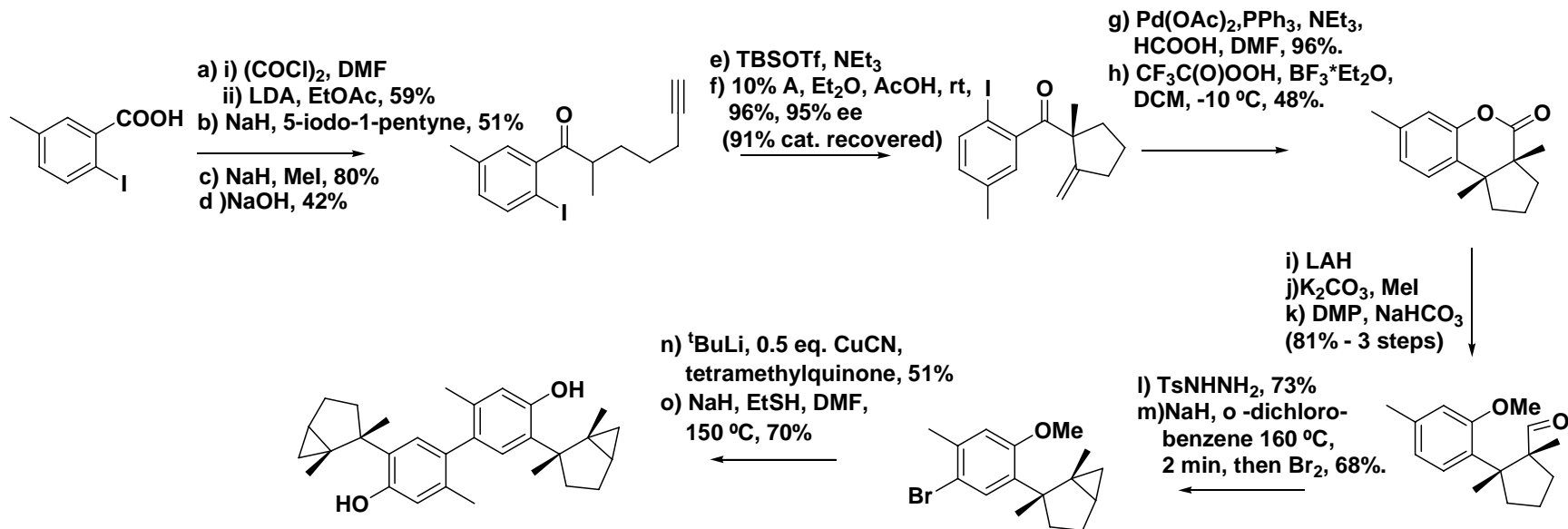
Synthesis of (+/-)-Epiglobulol

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



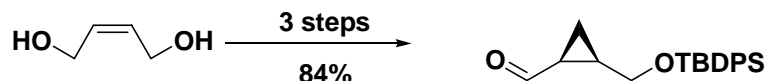
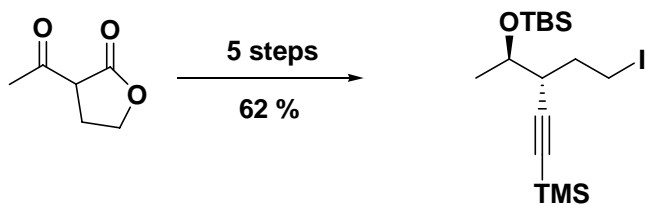
Total Synthesis of (-)-Laurebiphenyl

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

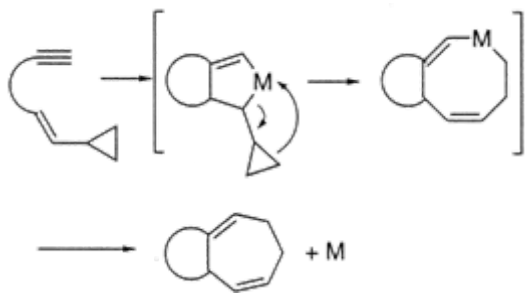


Total Synthesis of (-)-Pseudolaric Acid B

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

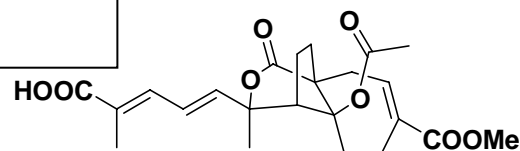
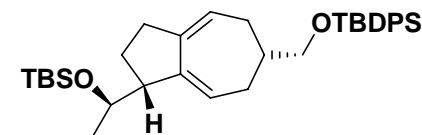
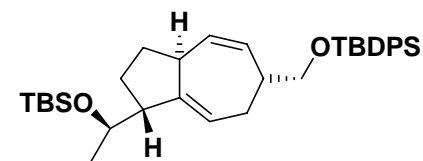
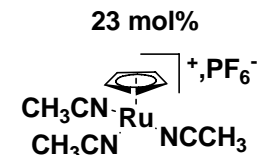
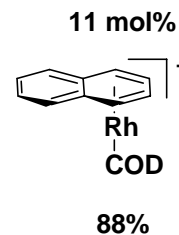
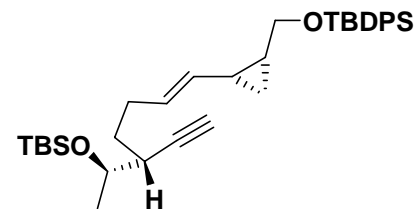


Mechanism:



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.

