Allenes: Preparation and Recent Application

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Dong Group Literature Talk
September 19, 2012

Outline

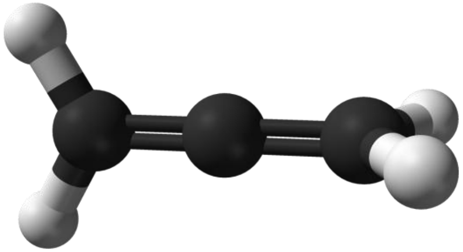
- Introduction
  - Overview

- Methods of Preparation
  - Elimination, Isomerization, Substitution
  - Homologation and Rearrangements
  - Transition Metal

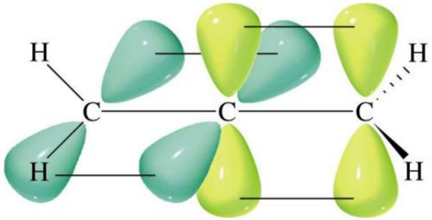
- Application in Catalytic and Asymmetric Syntheses
  - Selected Examples Toward Natural Product Synthesis

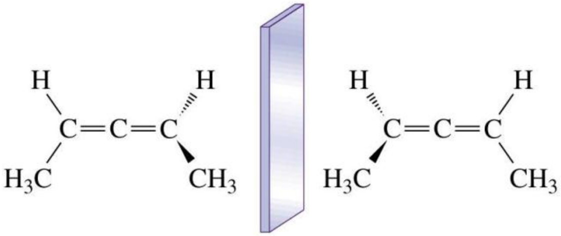
Allenes in Organic Synthesis, Wiley, New York, **1984**

What are Allenes?



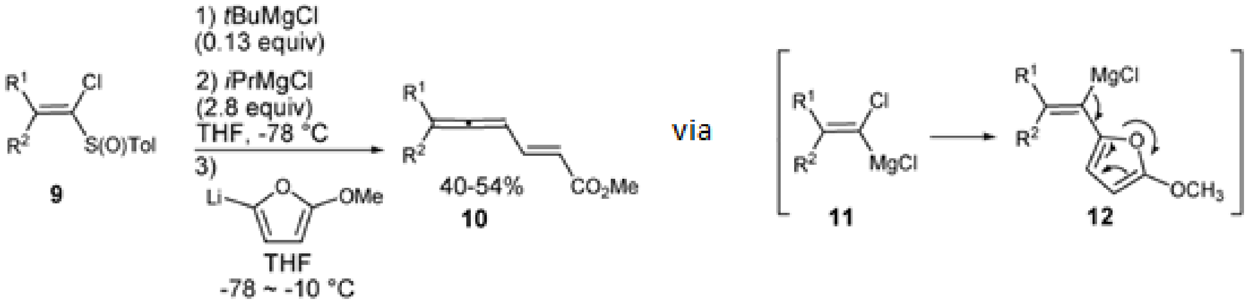
- Simplest class of cumulenes
- Unsaturation over three atoms allows unique flexibility for synthesis
- Higher reactivity than alkenes and alkynes
- Intrinsic axial chirality (elongated tetrahedral)

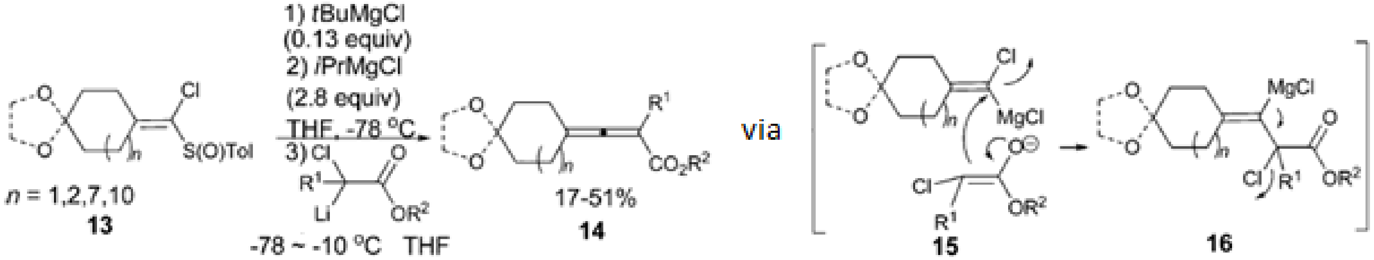


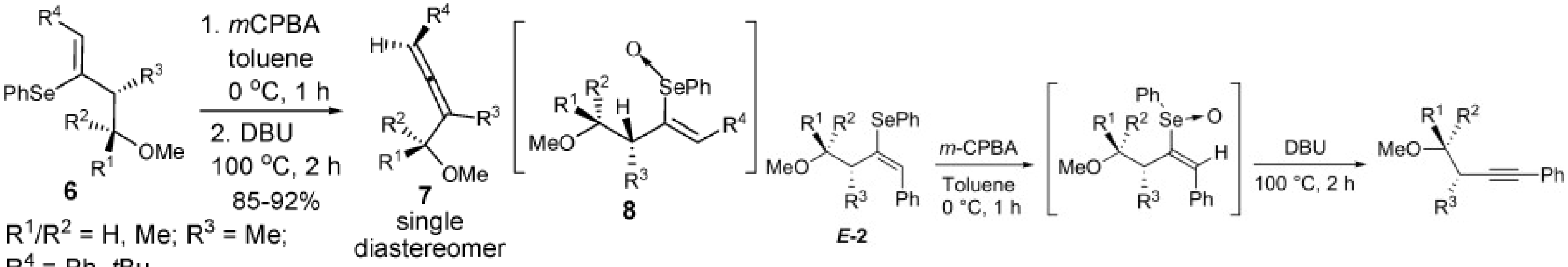


Honda, M. et al., *Tetrahedron*, **2009**, 65
Mori, N. et al., *Tetrahedron*, **2009**, 65
Satoh, T. et al., *Tet Lett*, **2009**, 50

Preparation from Alkenes







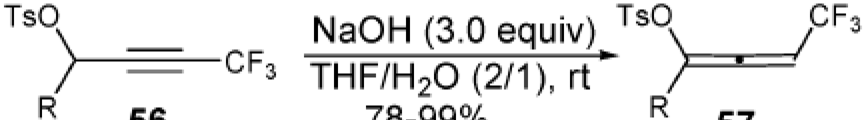
R^1/R^2 = H, Me; R^3 = Me;
R^4 = Ph, *t*Bu

Watanabe, Y. and Yamazaki, T, *J. Fluorine Chem.*, 2010, **131**
Liu, H, et al., *JACS*, 2009, **131**

Preparation from Alkynes

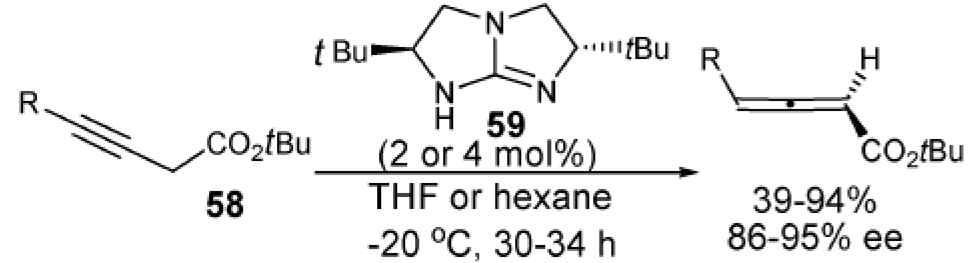
2-I **2-II**

FG: alkenyl, alkynyl, aryl, carbonyl, RO-, R_2N-, RS-, $PO(OEt)_2$-



56 **57**

R = $BnCH_2$, C_9H_{19}, *c*-Hex, *t*Bu, $BnO(CH_2)_2$, Ph(MOMO)CH



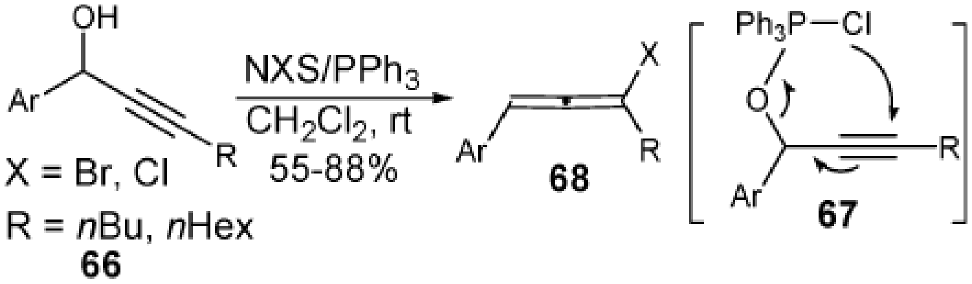
58 **59** **60**

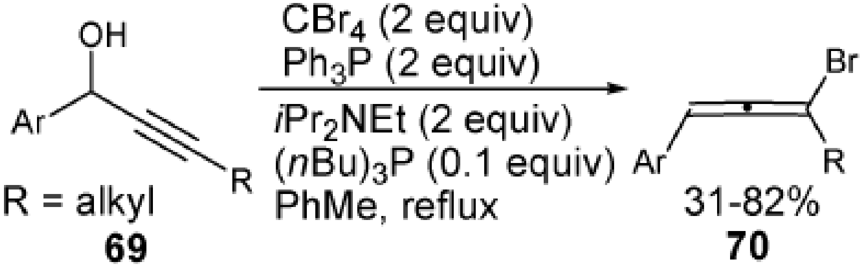
39-94%
86-95% ee

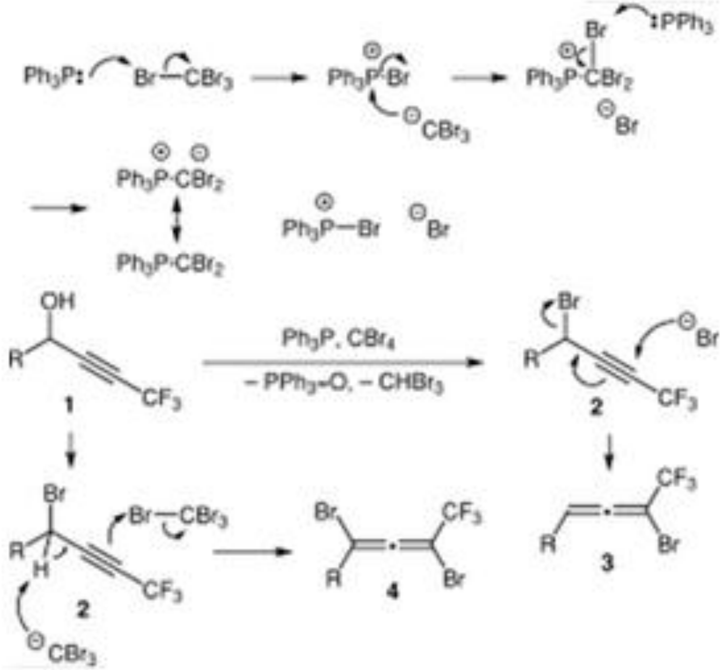
R = aryl, CH_2OH, $Me_2C(OH)$, $C(Me)_2(OBn)$, CH_2CbzNH, CH_2PhthN

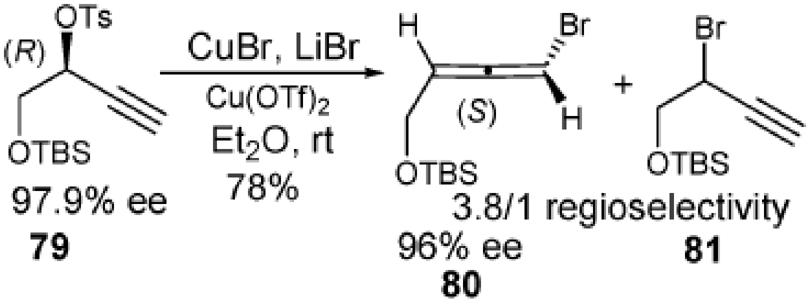
Watanabe, Y. and Yamazaki, T, *Synlett.*, 2009
Jian, Y.J., and Wu, Y., , *Synlett*, 2009

Preparation from Alkynes



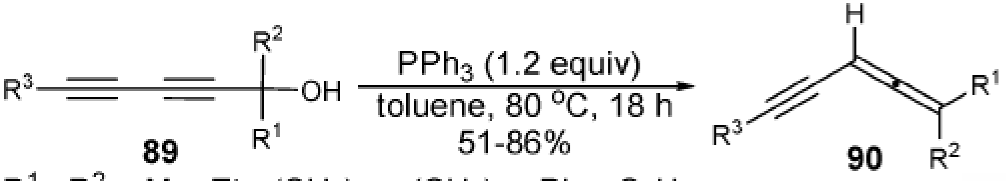






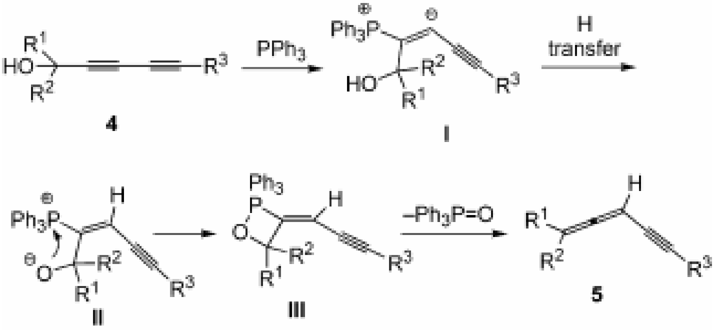
Sanz, R,, et al., *Synlett.*, 2009
Jiang, H., et al., , *Eur J Org Chem,* 2010

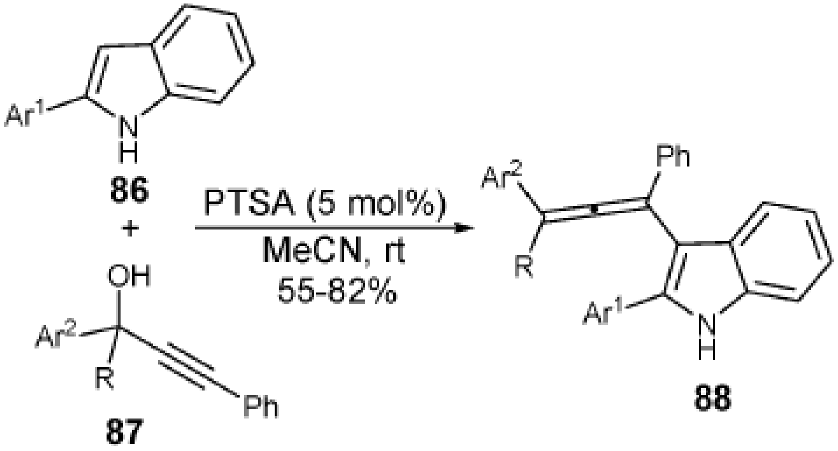
Alkynes - Substitution



89 **90**

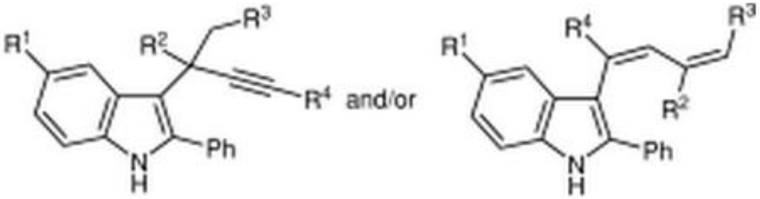
R^1, R^2 = Me, Et, -$(CH_2)_5$-, -$(CH_2)_6$-, Ph, $n$$C_6H_{13}$





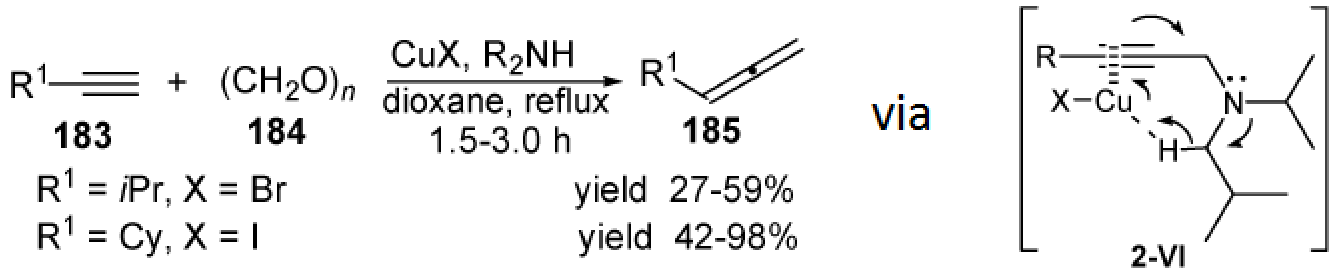
86
+
87
88

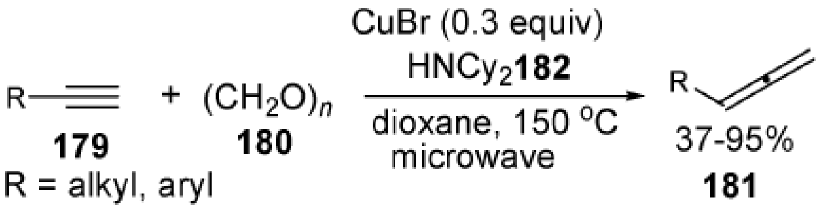
R = iPr, c-C_3H_5, c-C_4H_7, c-C_5H_9, c-C_6H_{11}

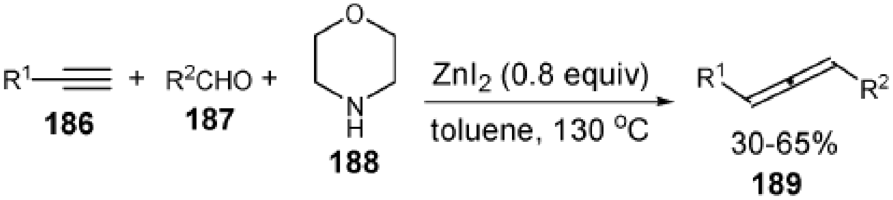


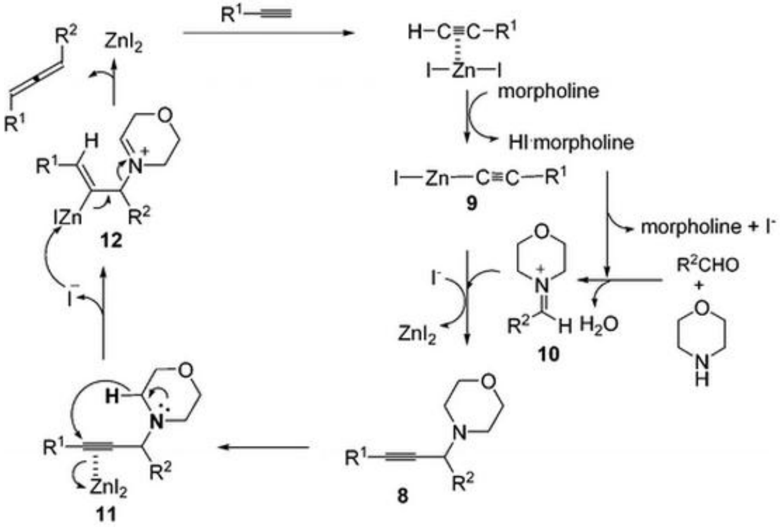
Crabbe, P., et al., *JACS Chem Comm*, 1979
Kuang, J., Ma, S., *J Org Chem*, 2009
Kuang, J., Ma, S., *JACS*, 2010, 132

Preparation from Alkynes



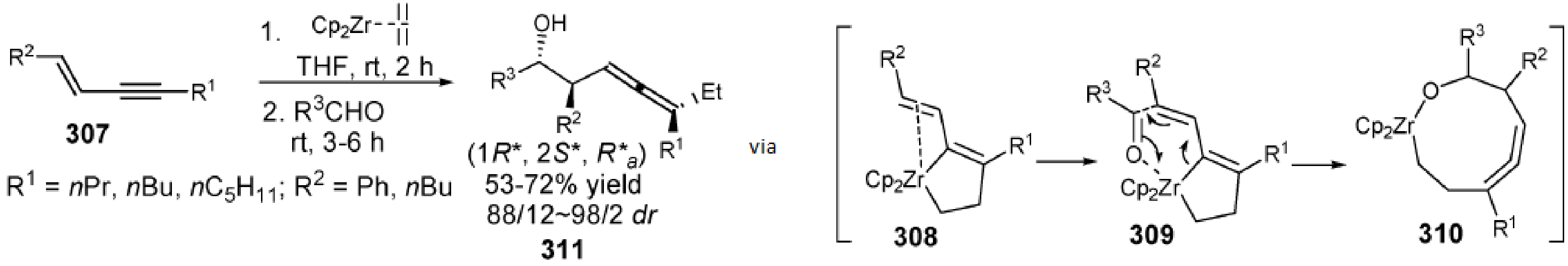


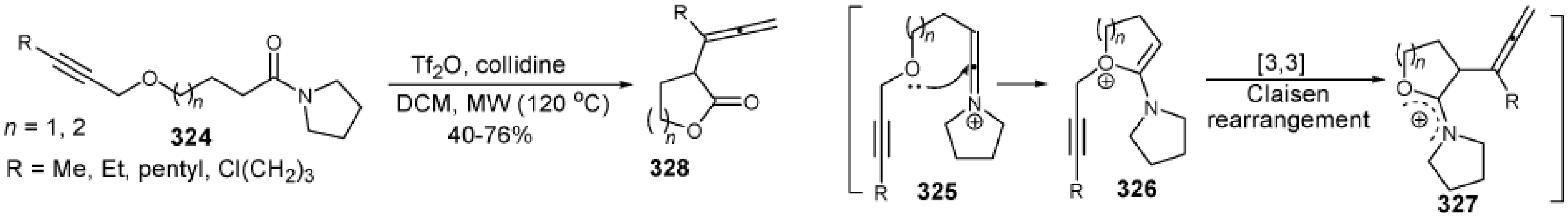


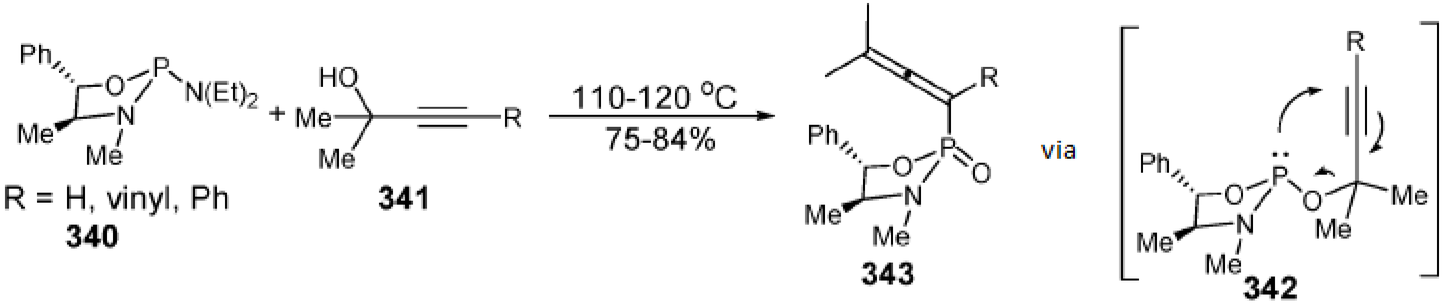


Zhou, Y., et al., *J Org Chem*, 2009
Madelaine, C., et al., *ACIE*, 2010
Nurkenov, O. A., et al., *Russ J Gen Chem* 2008

Preparation from Rearrangements

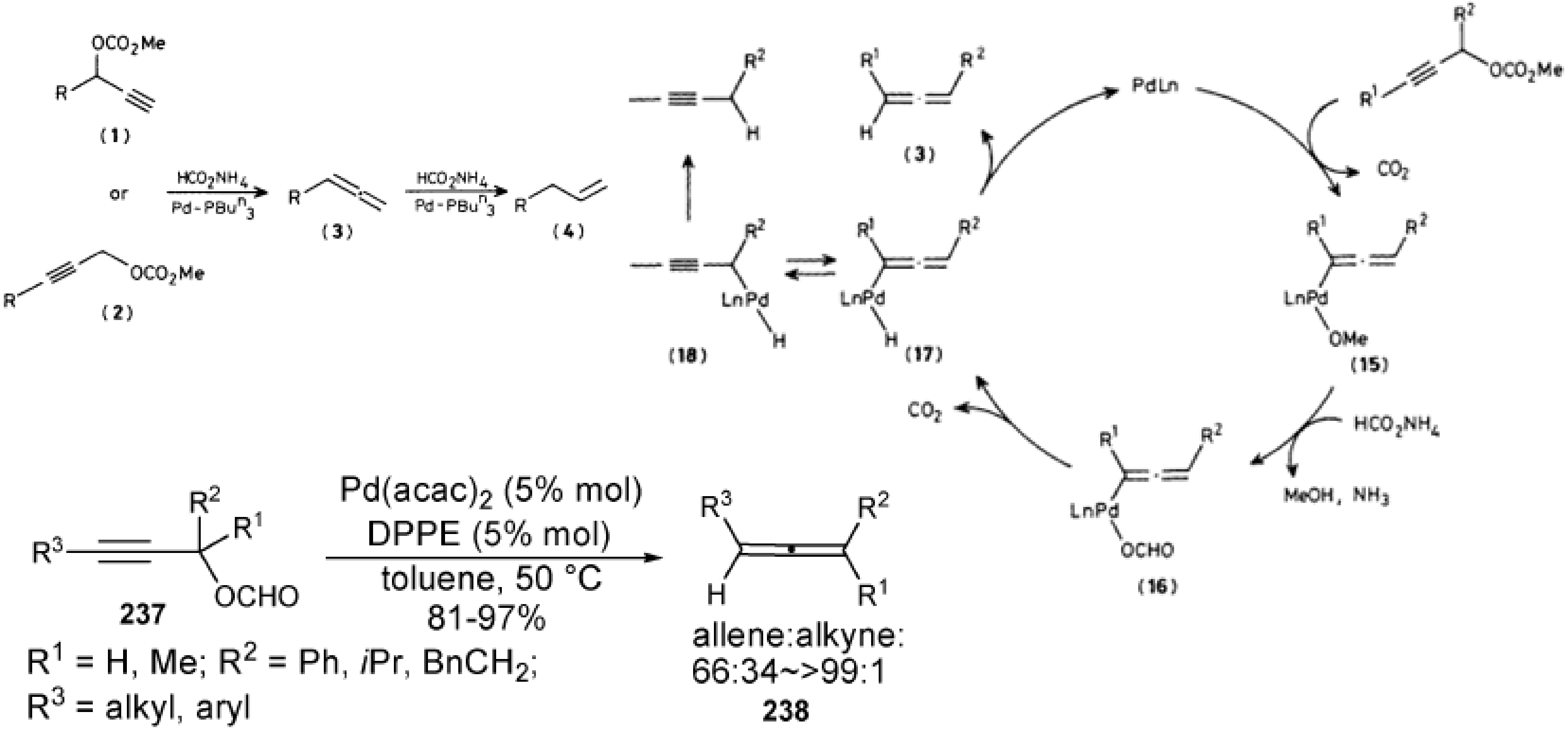






Ohmiya, H., et al., *Org Lett*, 2010
Tsuji, J., et al., *J Chem Soc Chem Comm*, 1986

Pd-Catalyzed Allene Formation



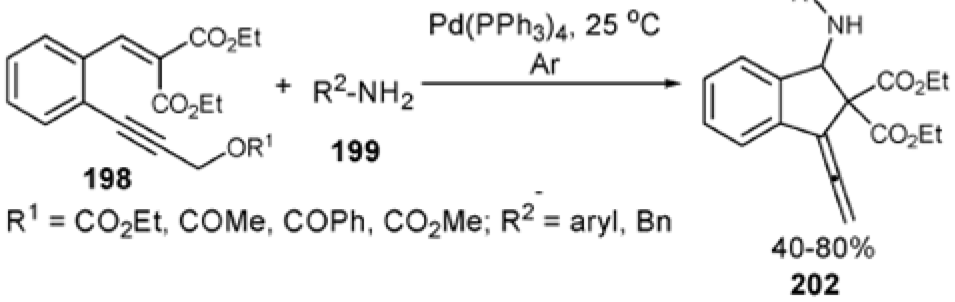
$Pd(acac)_2$ (5% mol)
DPPE (5% mol)
toluene, 50 °C
81-97%

R^1 = H, Me; R^2 = Ph, *i*Pr, $BnCH_2$;
R^3 = alkyl, aryl

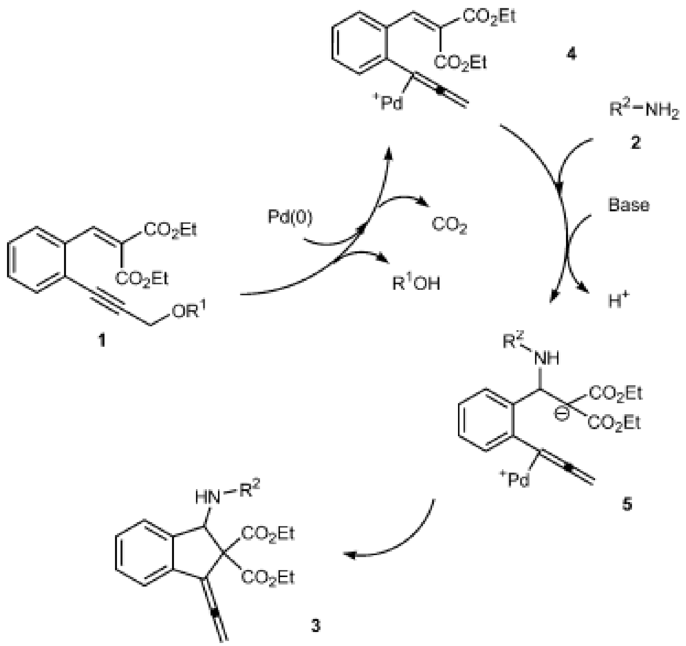
allene:alkyne:
66:34~>99:1

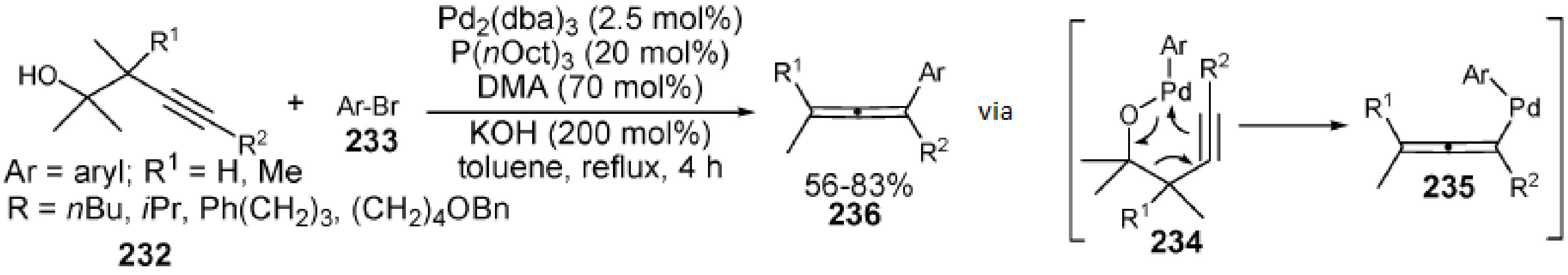
Shi, Y., et al., *Adv Synth Catal.*, 2009, **351**
Hayashi, S., et al., *JACS*, 2008, **130**

Pd Examples



R^1 = CO$_2$Et, COMe, COPh, CO$_2$Me; R^2 = aryl, Bn





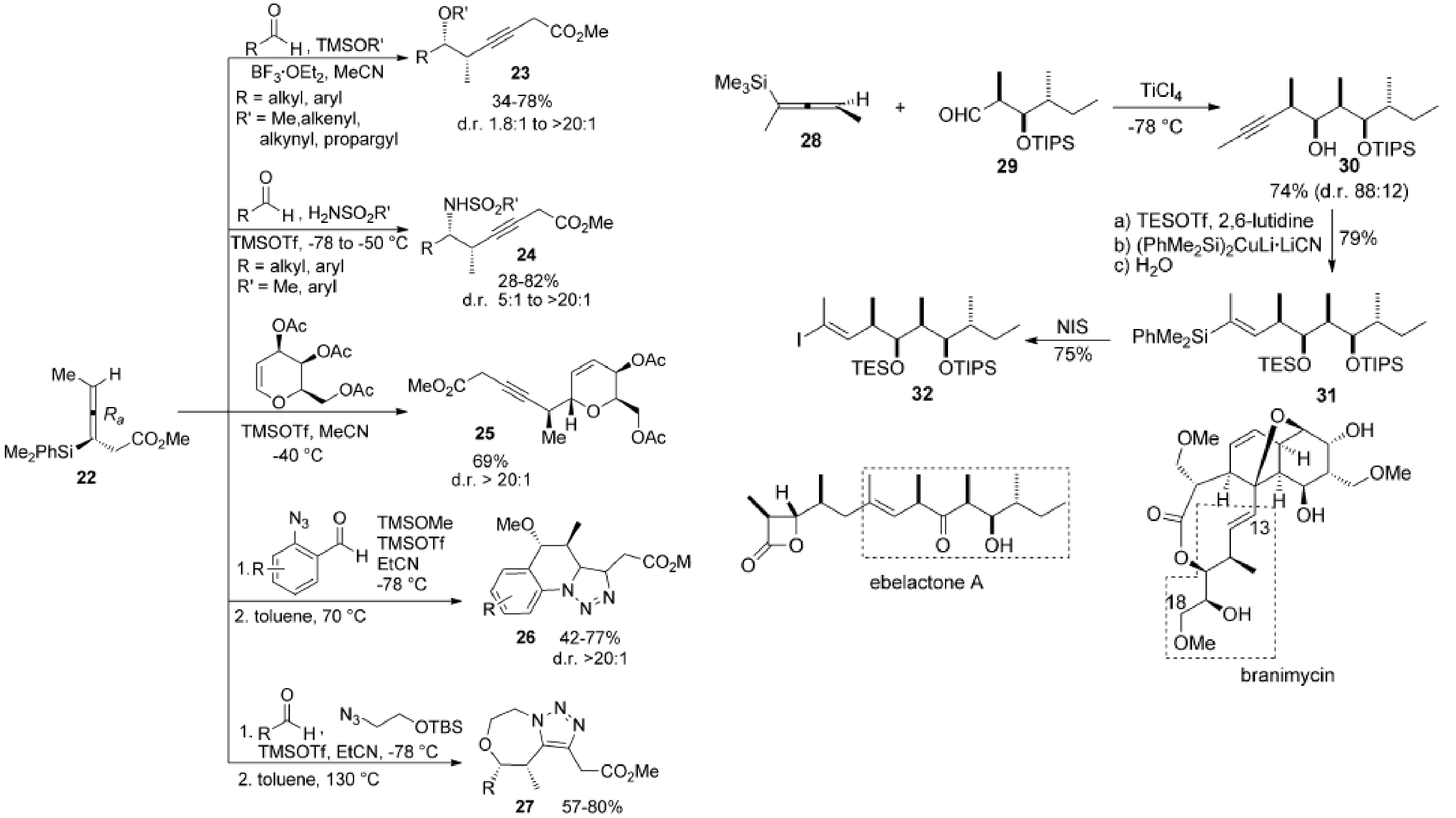
Ar = aryl; R^1 = H, Me
R = *n*Bu, *i*Pr, Ph(CH$_2$)$_3$, (CH$_2$)$_4$OBn
232

Why Bother Making Them?

- Recent explosion (> 2003) of catalytic and asymmetric reactions involving allenes (oftentimes applied toward making a natural product)
- Starting allenes may/may not have been discussed previously

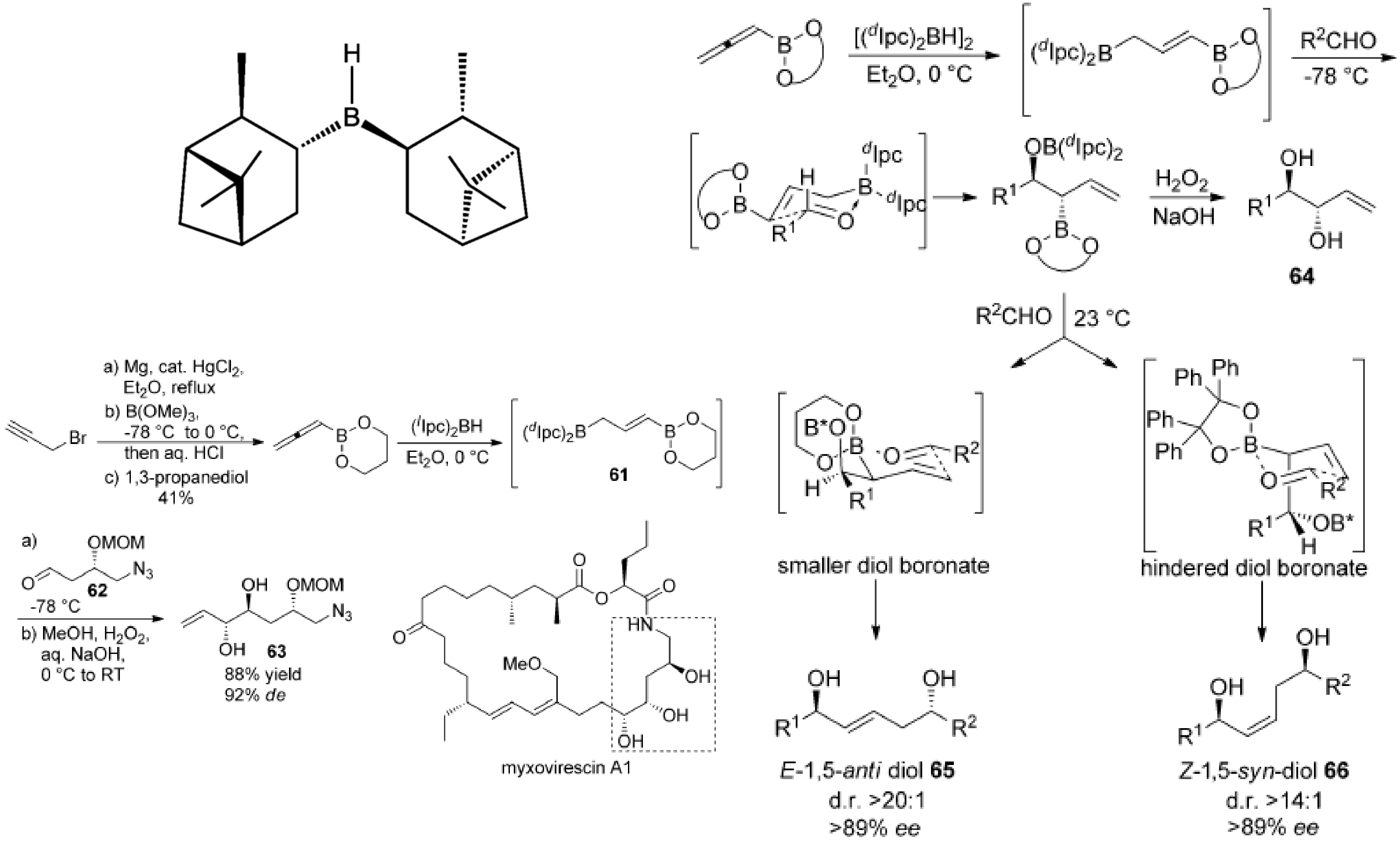
Brawn, R. A., et al., *Org Lett* 2010
Carrol, L., et al., *Org Biomol. Chem.* 2008
Fleming, I., *Pure Appl. Chem* 1990
Ilardi, E., et al., *Org Lett* **2008** 10

Reactions With Allenylsilane Reagents



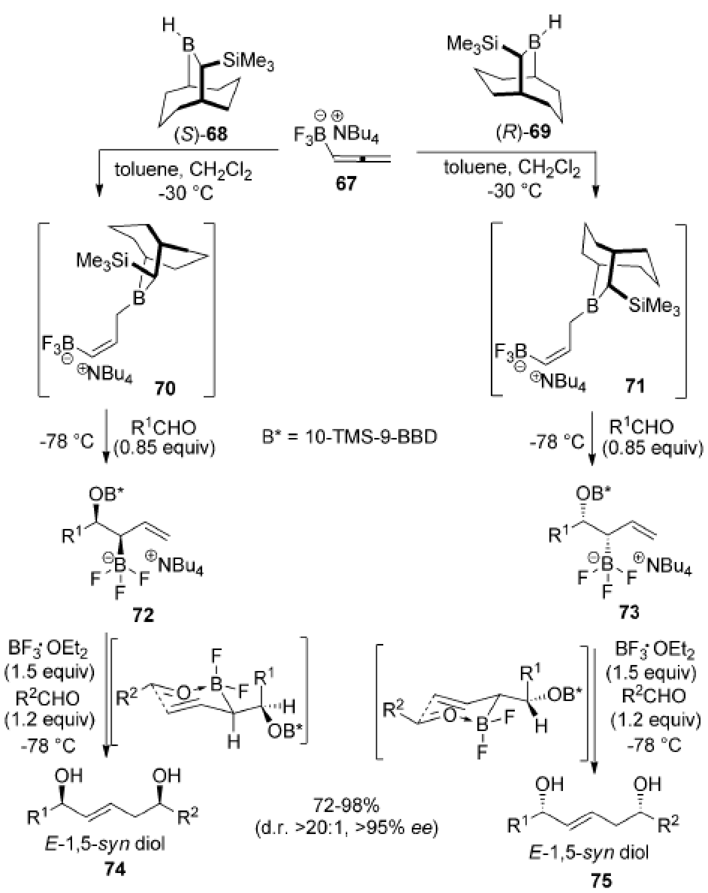
Furstner,, A., et al., *Chem Eur J* 2007
Flamme, E., Roush, W., *JACS* 2002
Kister, J., et al, *Org Lett* 2011

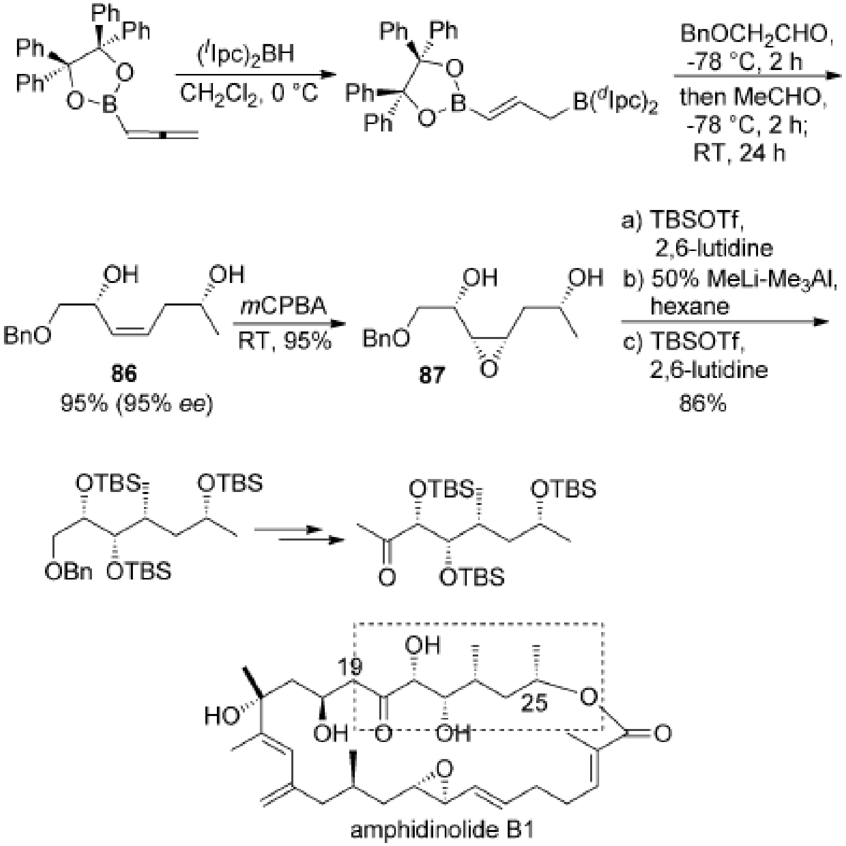
Allenylboranes



Flamme, E., Roush, W., *Org Lett*, 2005
Hicks, J.D., et al., *Org Lett* 2005

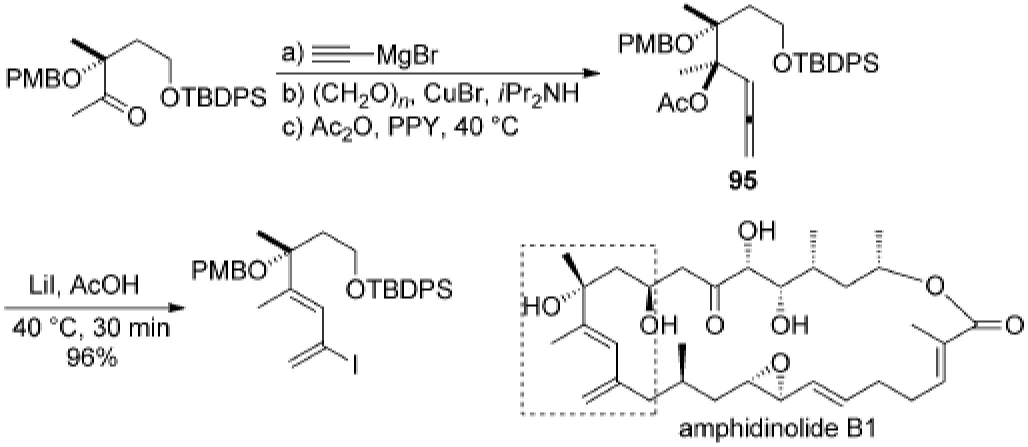
Improvements to 1,5 Diols

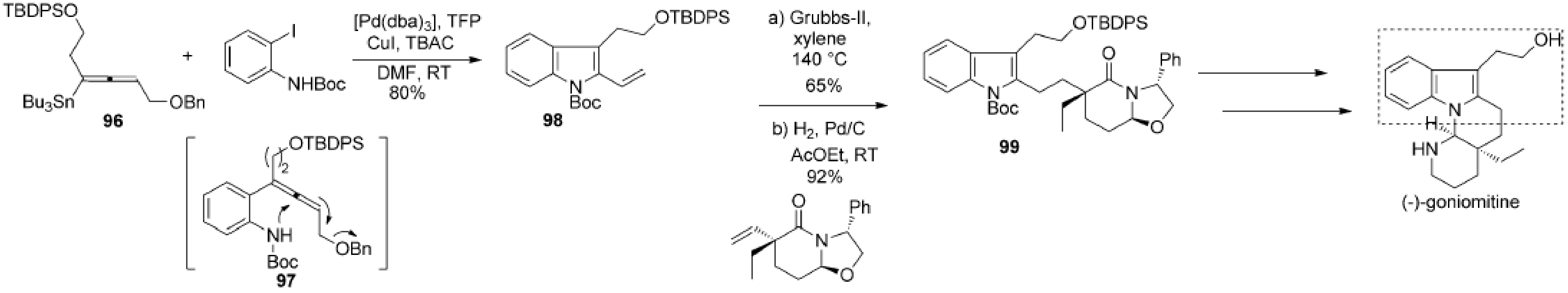




Ma, S., Wang, G., *Tet Lett* 2002
Mukai, C., Takahashi Y., *Org Lett 2005*
Mizutani, M., et al., *Org Lett* 2011

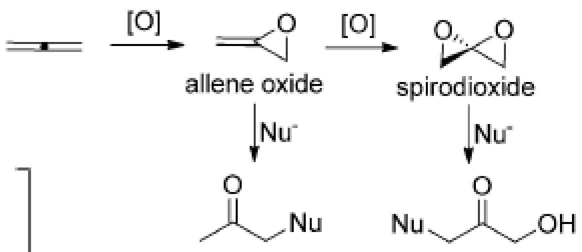
Allenes with an a-Functional Group

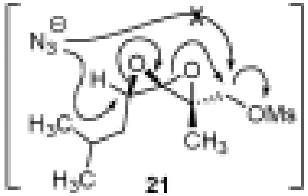


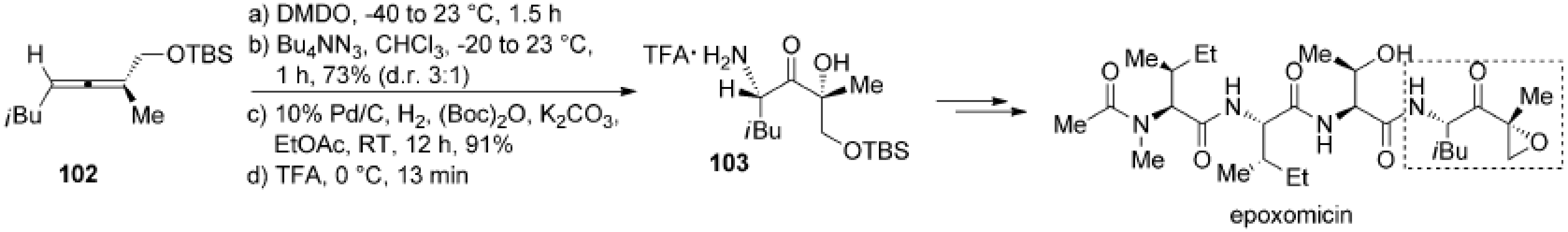


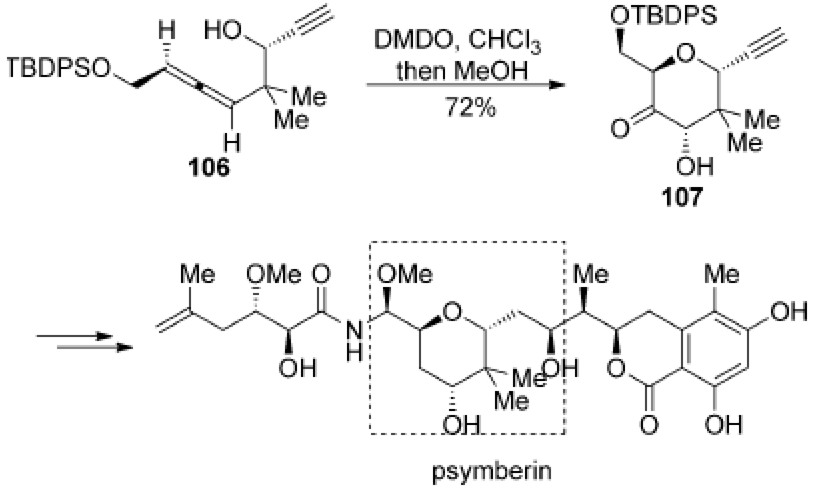
Katukojvala, S., et al., *JACS* 2004, 126
Shangguan, N., *Org Lett.* 2007, 9

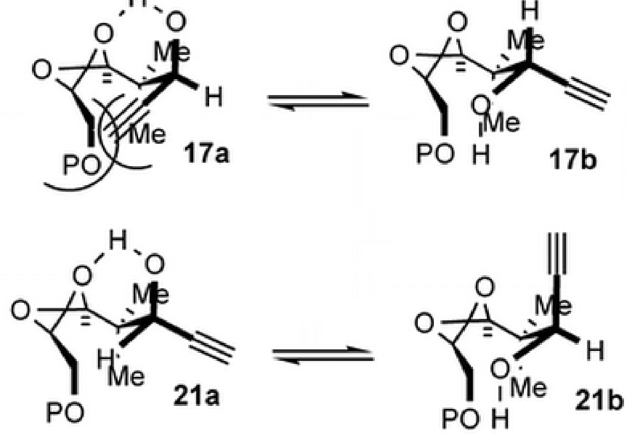
Epoxidations





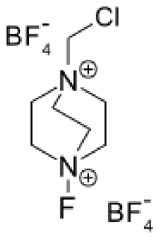




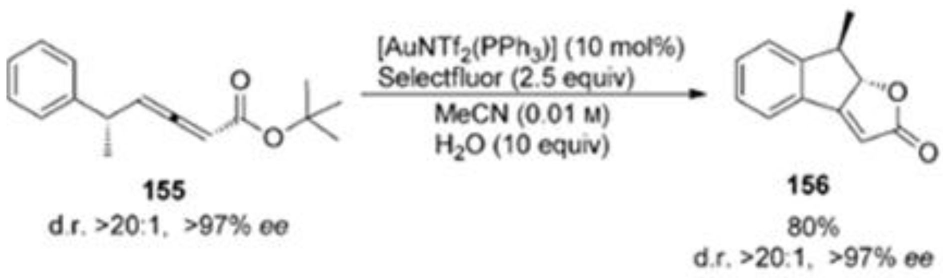


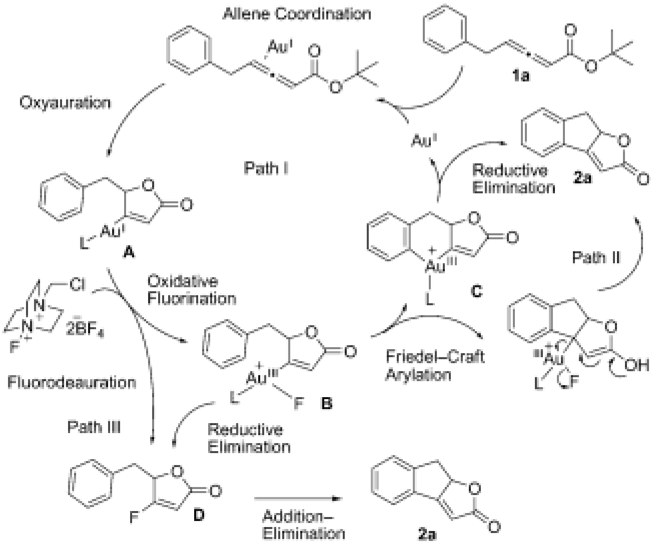
P = TBDPS, TBS, MOM

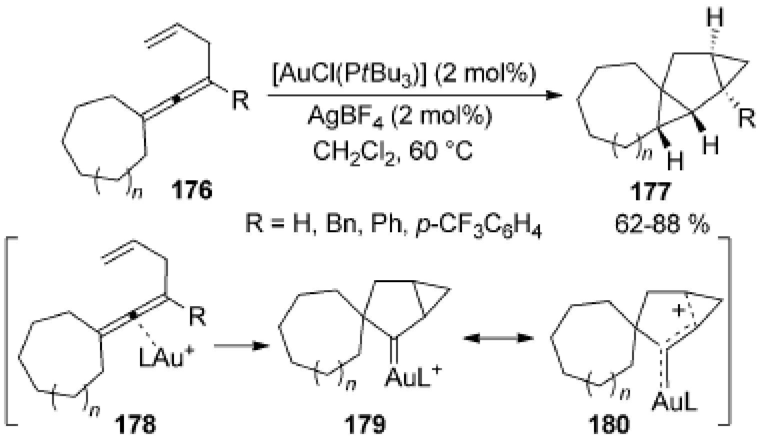
Hopkinson, M., et al., *Chem Eur J*, 2010
Horino, Y., and Toste, D., *JACS* 2009

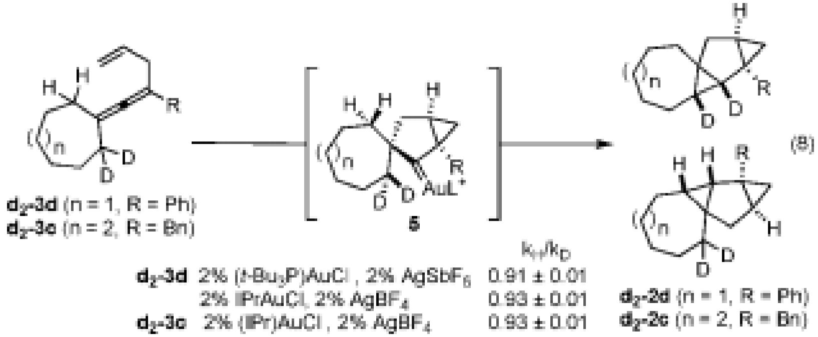


Au Cyclizations



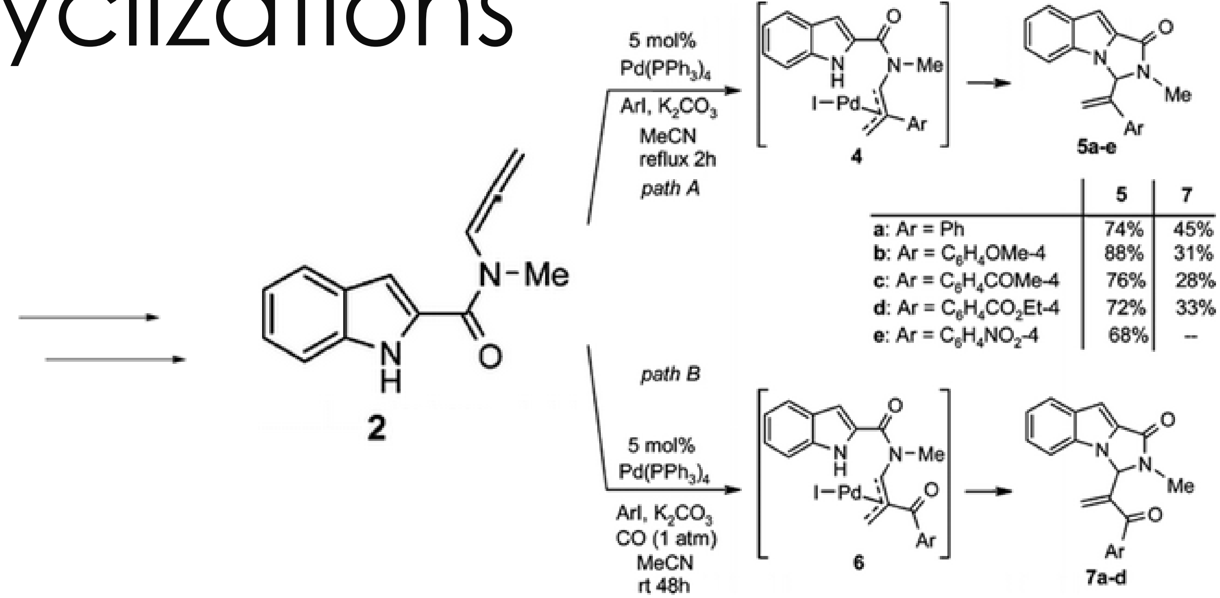




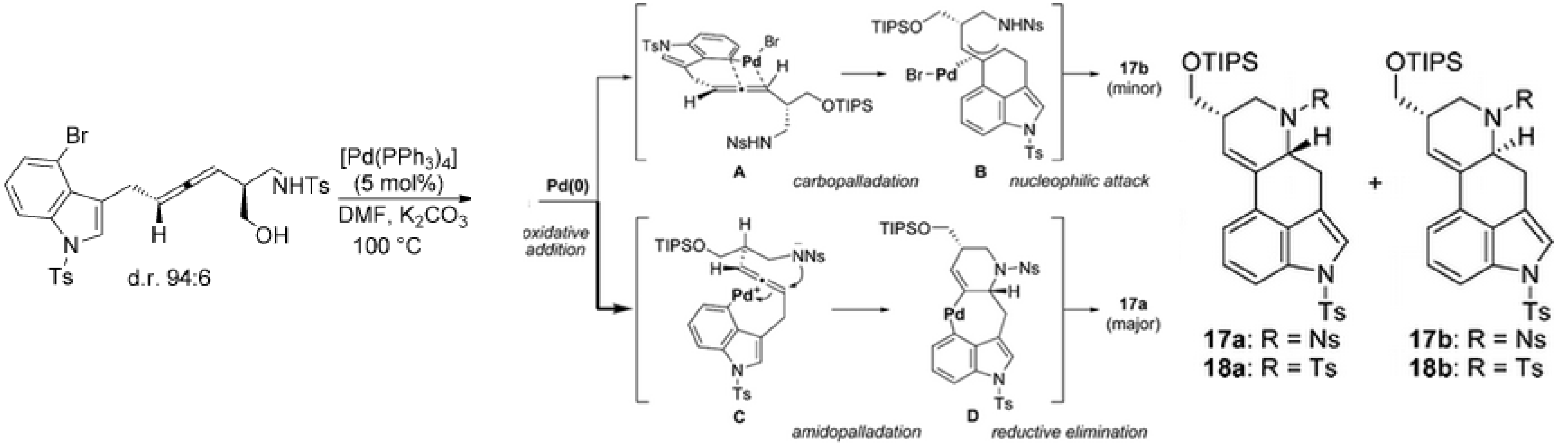


Li, M., Dixon, D. J., *Org Lett*. 2010, 12
Beccalli, E. M., et al., *J Org Chem* 2010, 75
Inuki, S., et al., *Org Lett* 2008, *10*

Pd Cyclizations

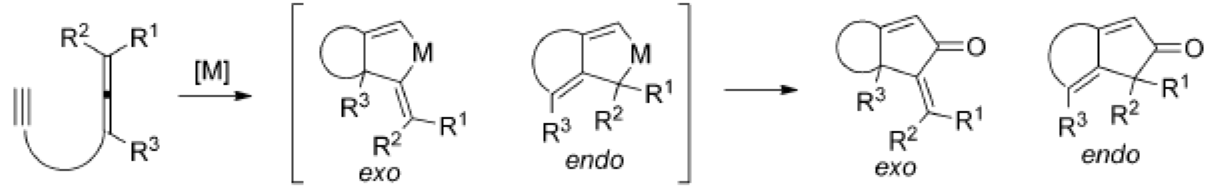


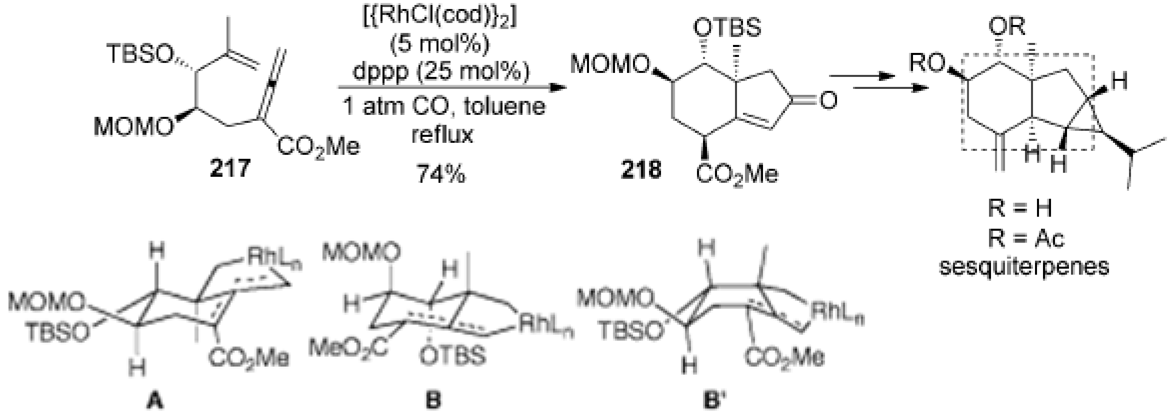
	5	7
a: Ar = Ph	74%	45%
b: Ar = C_6H_4OMe-4	88%	31%
c: Ar = C_6H_4COMe-4	76%	28%
d: Ar = $C_6H_4CO_2Et$-4	72%	33%
e: Ar = $C_6H_4NO_2$-4	68%	--

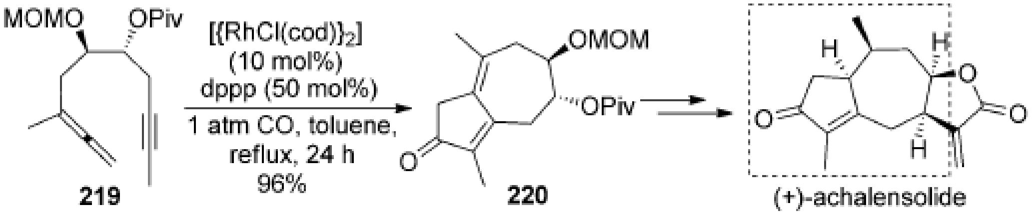


Hayashi, Y., *Org Lett*, 2008
Hirose, T., et al., *J Org Chem 2008*

Pauson Khand Cyclizations



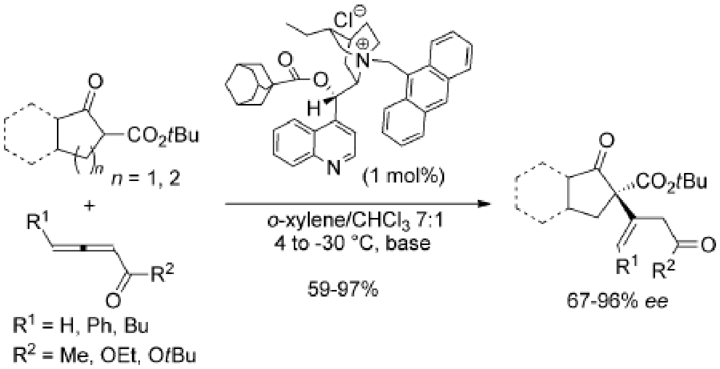


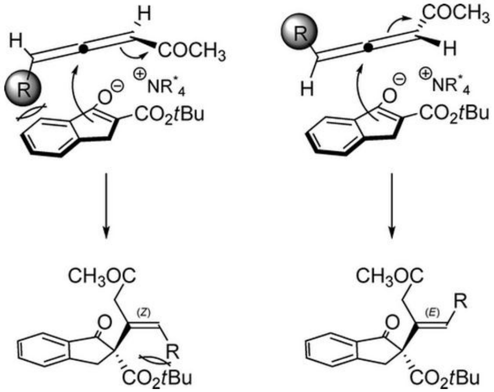


Elsner, P., et al., *JACS* 2008 130
Fu, C., Chen, G., Ma, S., *Chem Commun* 2005

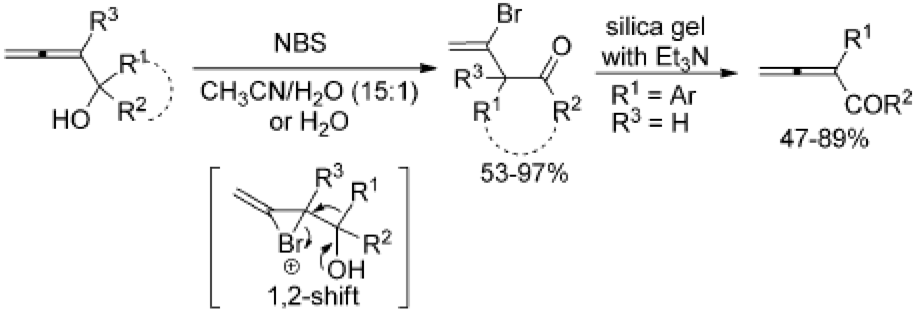
Future Work

- Nucleophilic Addition





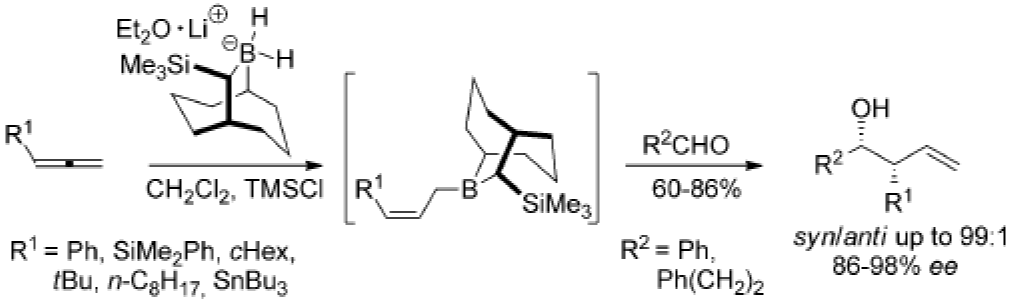
- Electrophilic Addition



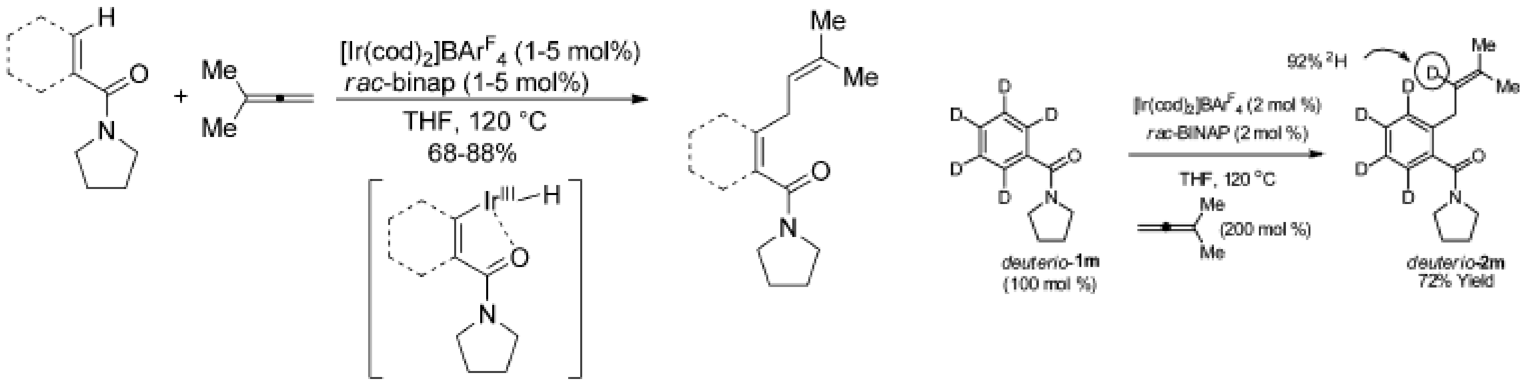
Kister, J., Roush, W., et al., *JACS* 2009
Zhang, Y. J., et al., *Org Lett*, 2009

Future Work

- Hydroborations



- C-H Bond Activation



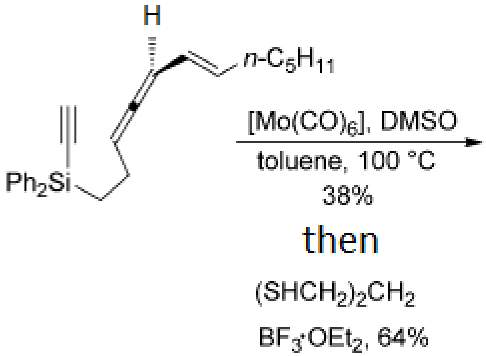
Conclusions

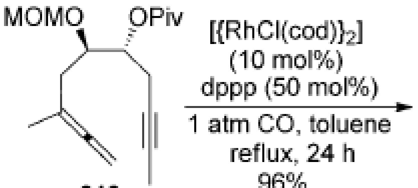
- Quickly becoming an irreplaceable class of compounds; no longer “chemist curiosities”

- Adaptation of “classical reactions” with wider substrate scope and milder reaction conditions.

- Remaining challenges:
  - Diverse reactivity still unpredictable (substituent effect)
  - Limited number of asymmetric reactions
  - Extensive structural and mechanistic studies still needed to elucidate reactivity and stereocontrol

Thank You! Questions!





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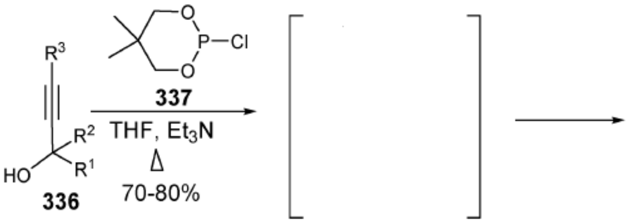
R = H, Me, *i*Pr; P^1 = Mts, Ts; n = 1, 2

X = NTs, NNs, O, $C(CO_2Et)_2$, *o*-C_6H_5NHTs



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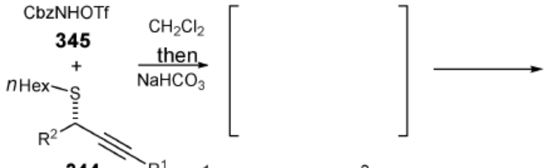

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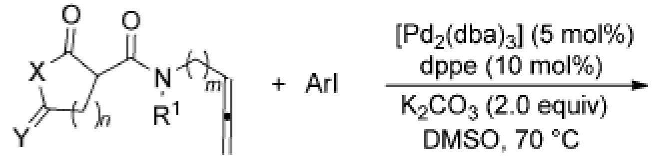
R^1 = H, CH_2OH; R^2 = Et, *i*Pr, Bn



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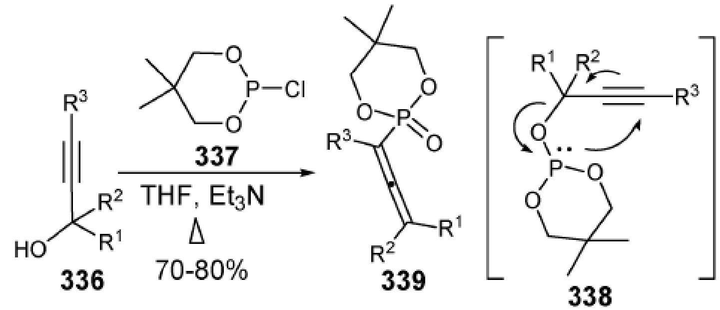
R^1 = Me, Et, Bn, Pr, allyl

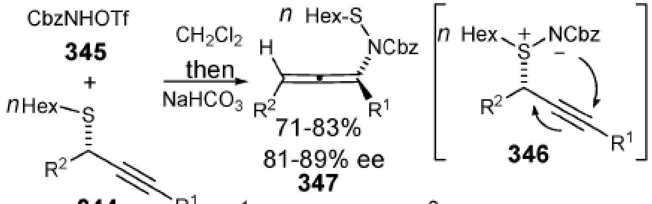
n = 1 to 4, m = 1 to 3

X = CH_2, NBn, NMe, NBoc; Y = O, H

Answers

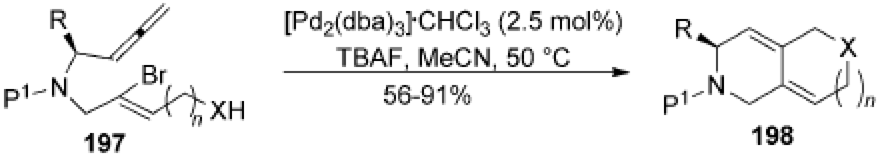


336 **339** **338**



344 **347** **346**

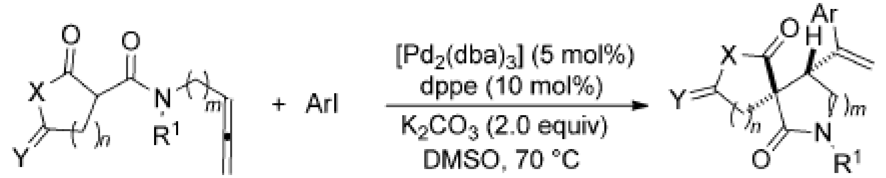
R^1 = H, CH$_2$OH; R^2 = Et, *i*Pr, Bn



197 **198**

R = H, Me, *i*Pr; P^1 = Mts, Ts; *n* = 1, 2

X = NTs, NNs, O, C(CO$_2$Et)$_2$, *o*-C$_6$H$_5$NHTs



199 **200**

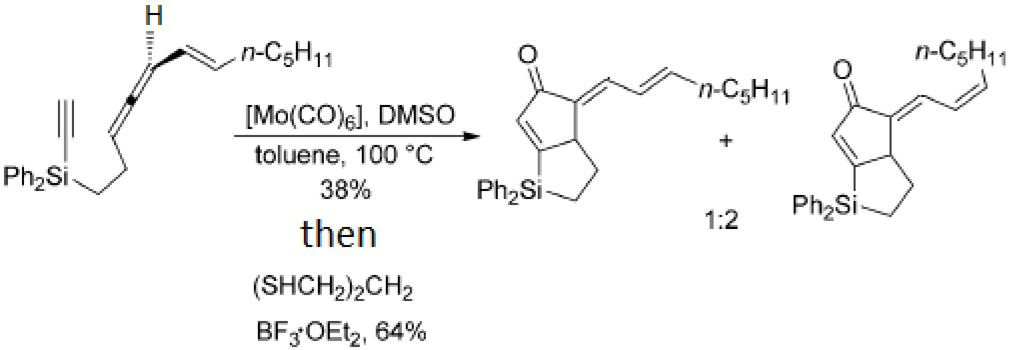
R^1 = Me, Et, Bn, Pr, allyl

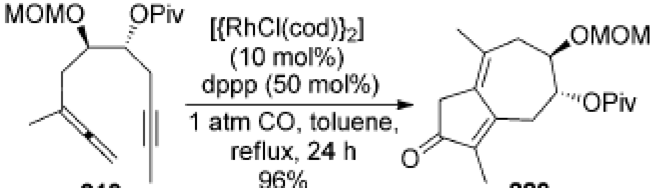
n = 1 to 4, *m* = 1 to 3

X = CH$_2$, NBn, NMe, NBoc; Y = O, H

50-86% yield

d.r. 3:1 to 47:1





219 **220**