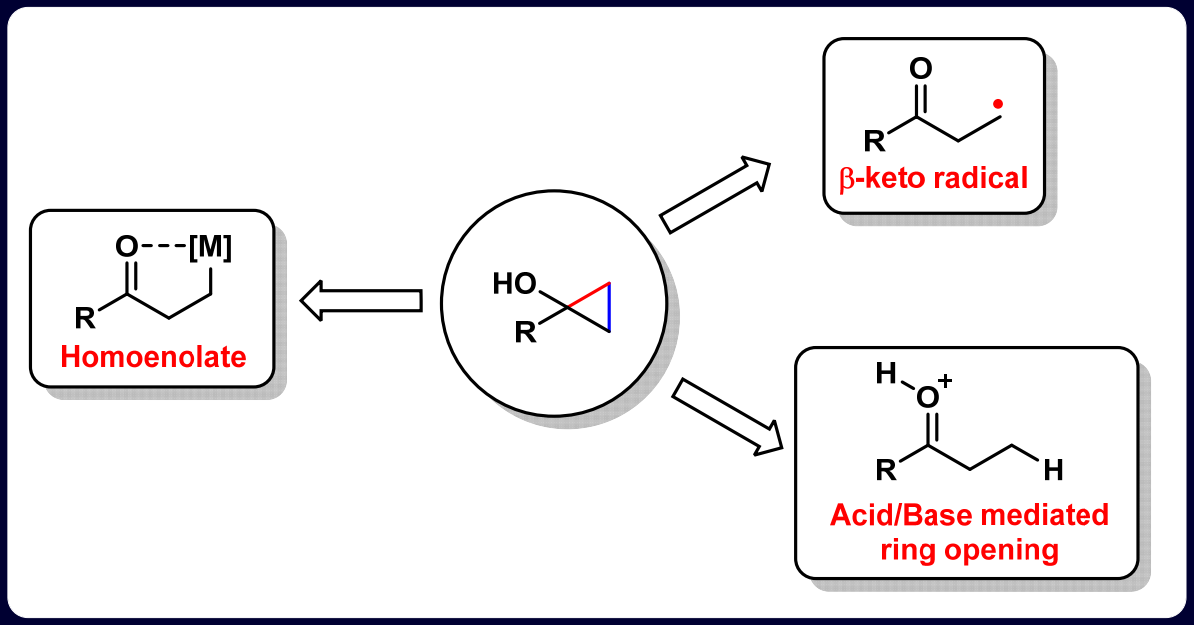
Selective Carbon–Carbon Bond Cleavage of Cyclopropanols



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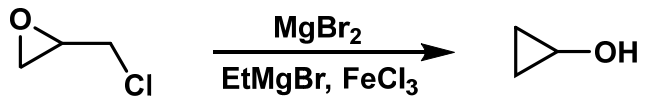
Peking University
Dec. 26th . 2020

Content

- *Introduction*
- *Metal Homoenolates*
- *β-keto Radicals*
- *Acid/Base-Mediated Ring Opening*
- *Metal-catalyzed C-C Cleavage*
- *Donor-acceptor Cyclopropanols*
- *Summary & Acknowledgements*

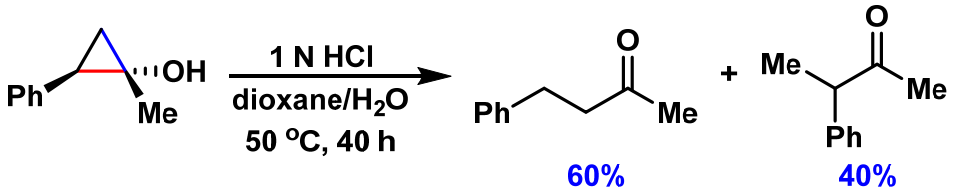
Introduction

- *1942, Cottle, 1st synthesis*

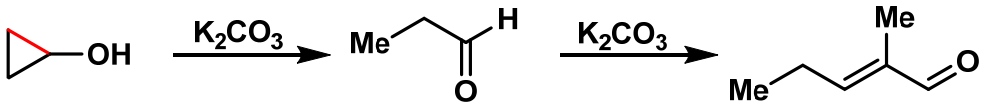


J. Am. Chem. Soc. **1942**, *64*, 484.

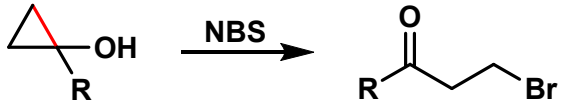
- *Acid/Base-Mediated Ring Opening*



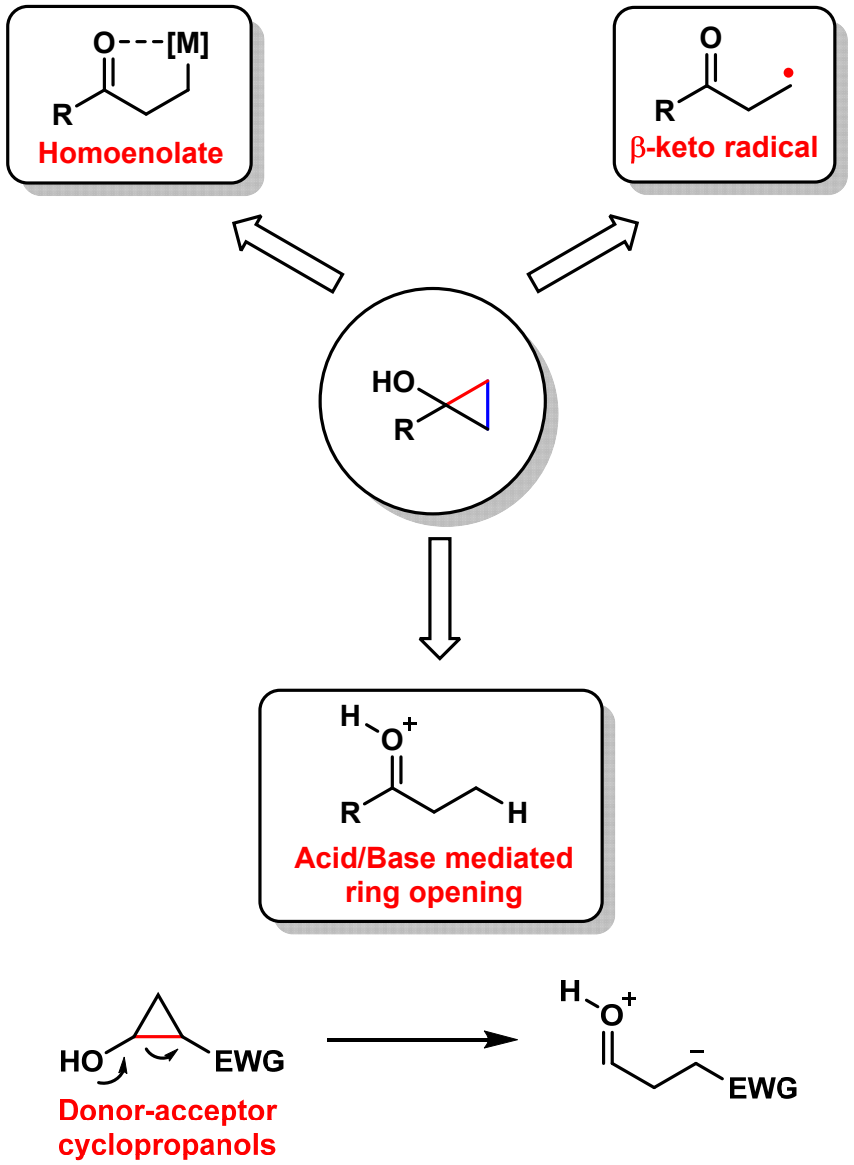
J. Am. Chem. Soc. **1966**, *88*, 3347.



- *Electrophilic Halogenation*

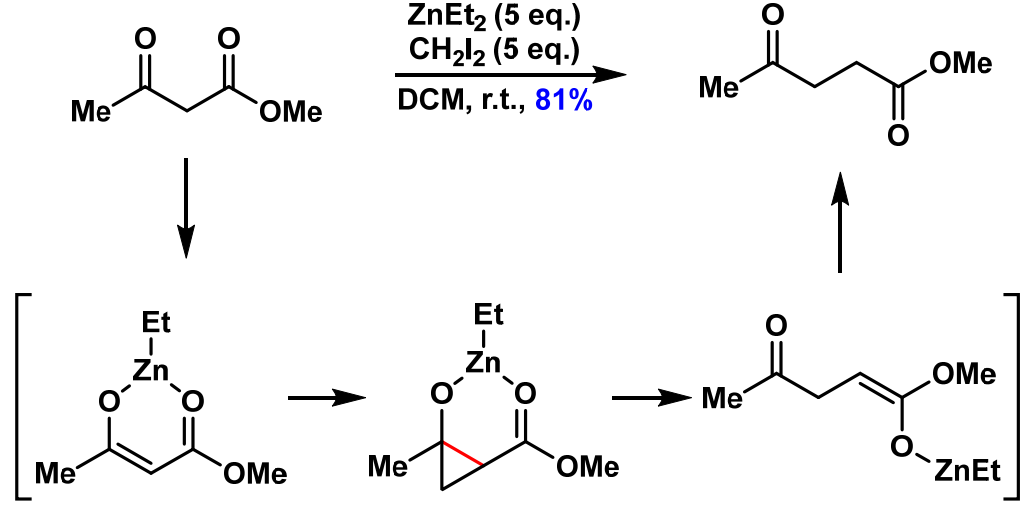


J. Am. Chem. Soc. **1968**, *90*, 1830.

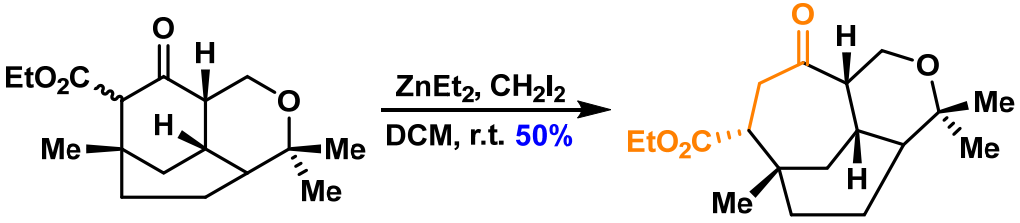


Metal Homoenolates

- *Ring opening of Donor-Acceptor Cyclopropyl alcohols*
  - *β-Keto Esters to γ-Keto Esters*

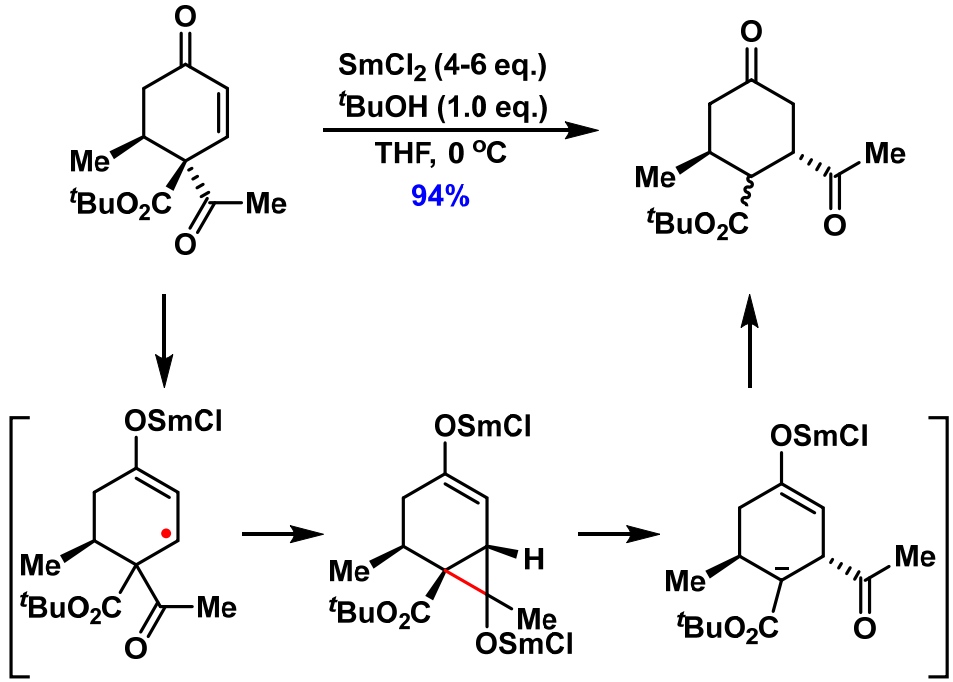


J. Org. Chem. **1997**, *62*, 6444.

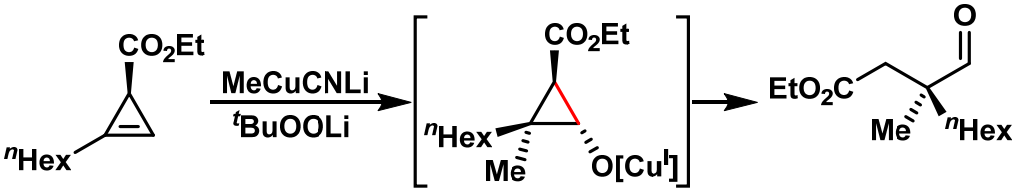


Org. Lett. **2005**, *7*, 1327.

  - *Retro-aldol ring-opening reaction*



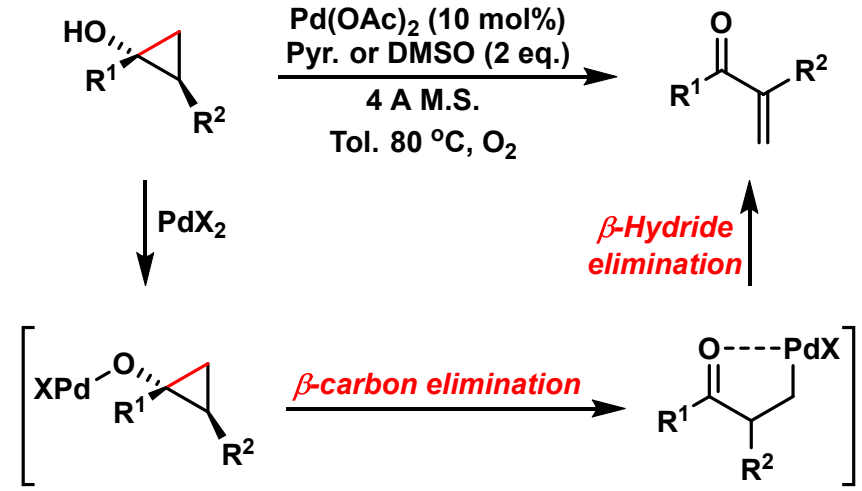
J. Org. Chem. **2005**, *70*, 1497.

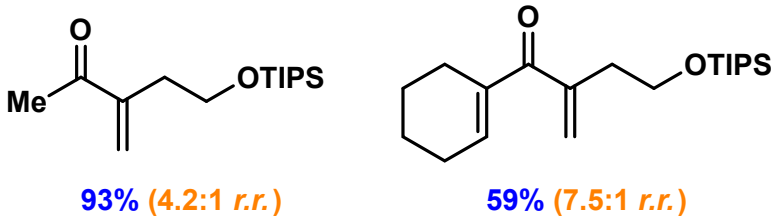


Angew. Chem. Int. Ed. **2013**, *52*, 5333.

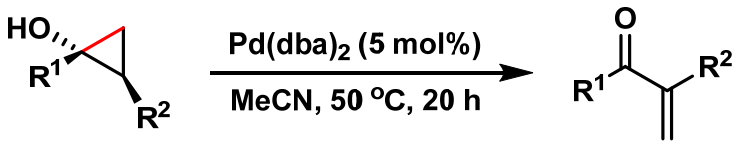
Metal Homoenolates

➢ 2000, Pd-catalyzed ring-opening



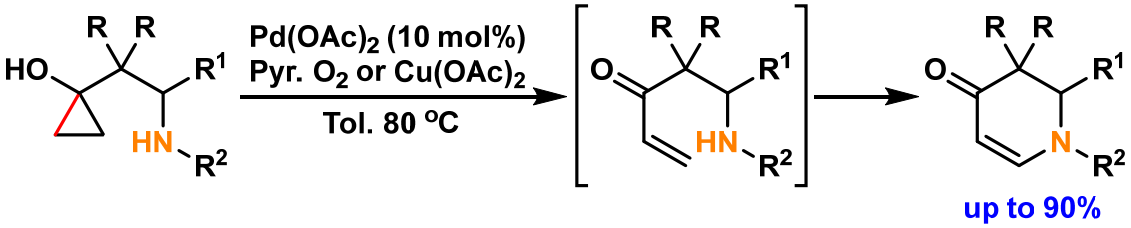


Org. Lett. **2000**, *2*, 147.



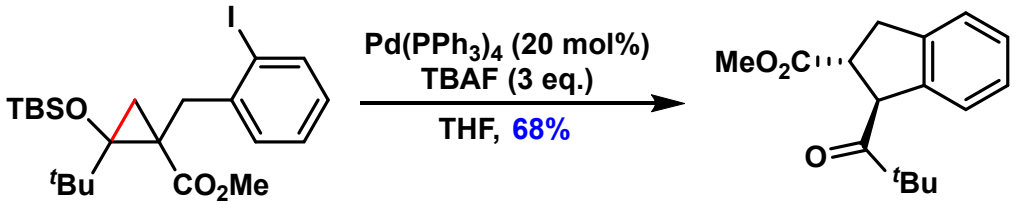
Synlett, **2000**, 629.

➢ Domino type Process

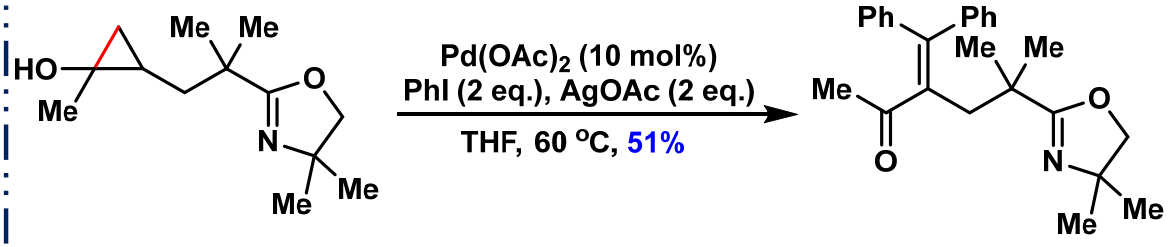


J. Org. Chem. **2005**, *70*, 5636.

➢ Heck-type arylation



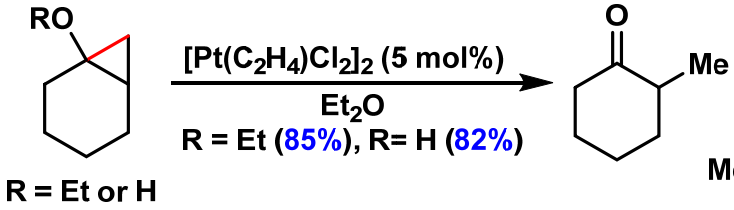
Synlett, **1996**, 533.



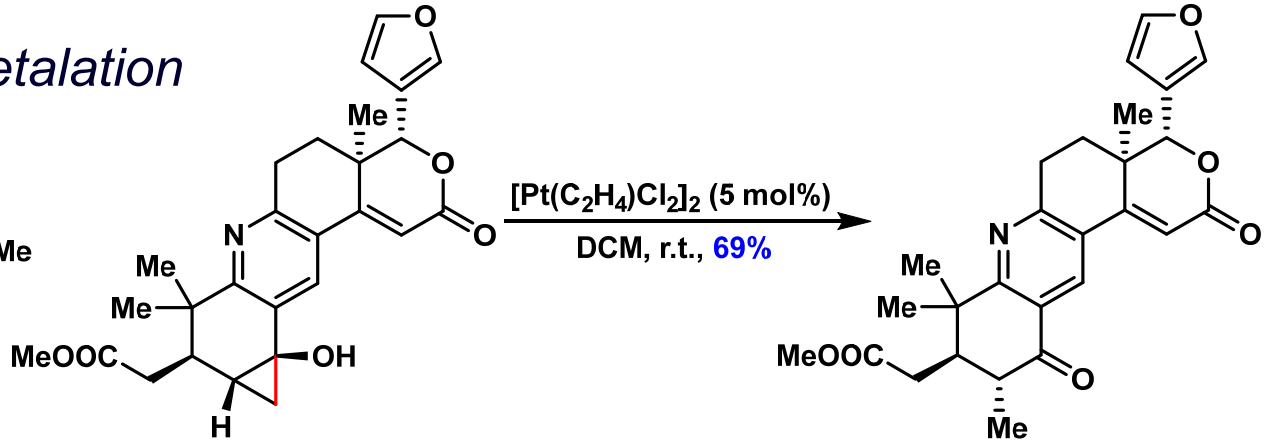
Tetrahedron. **2018**, *74*, 1078.

Metal Homoenolates

- *Ring opening and protodemetalation*
  - *Pt-catalyzed*

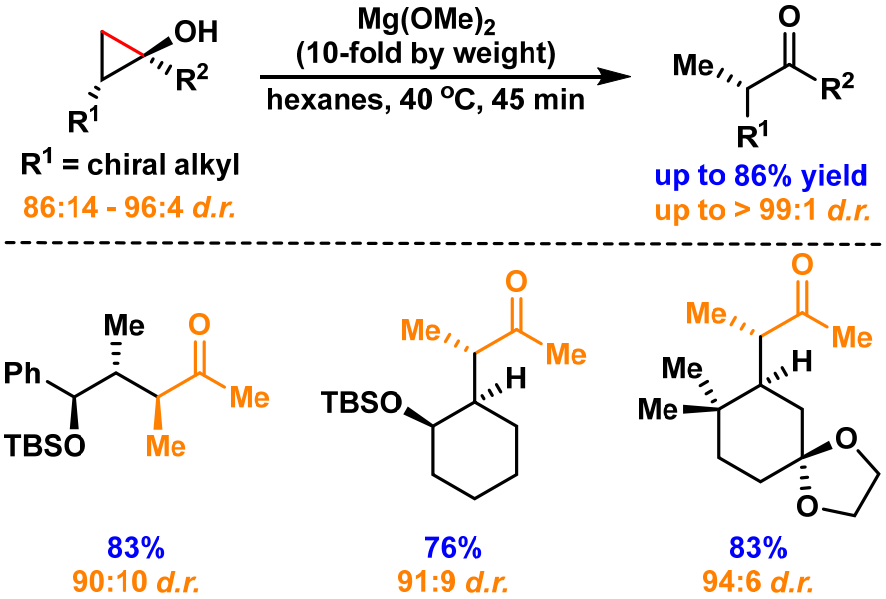


Organometallics, **1996**, *15*, 3902.



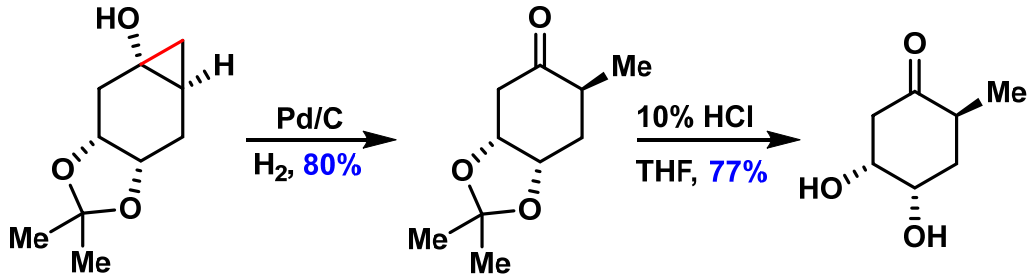
J. Am. Chem. Soc. **2018**, *140*, 2062.

  - *Mg-catalyzed*



Chem. Commun. **2018**, *54*, 2800.

  - *Pd-catalyzed*



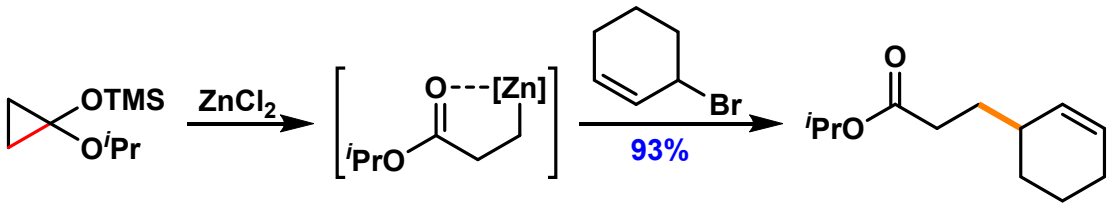
Synthesis, **2008**, 3171.

Ti?
This process is reversible an lies toward the side of the Ti cyclopropoxide.

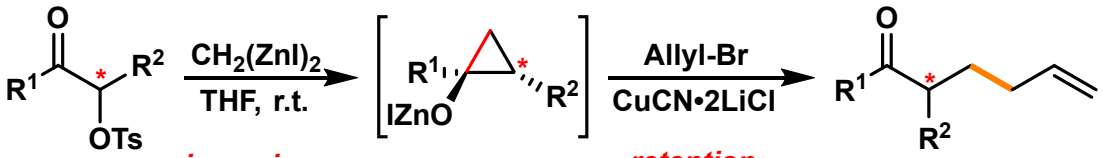
Can. J. Chem. **2006**, *84*, 1208.

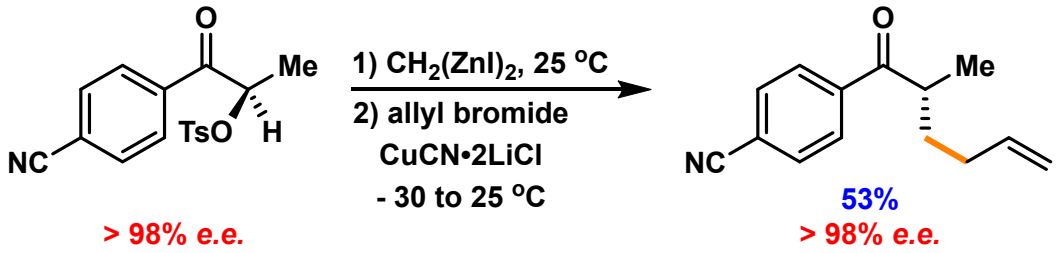
Metal Homoenolates

- *β-Functionalization with C(sp^3)−X Electrophiles*
  - *Allylation*

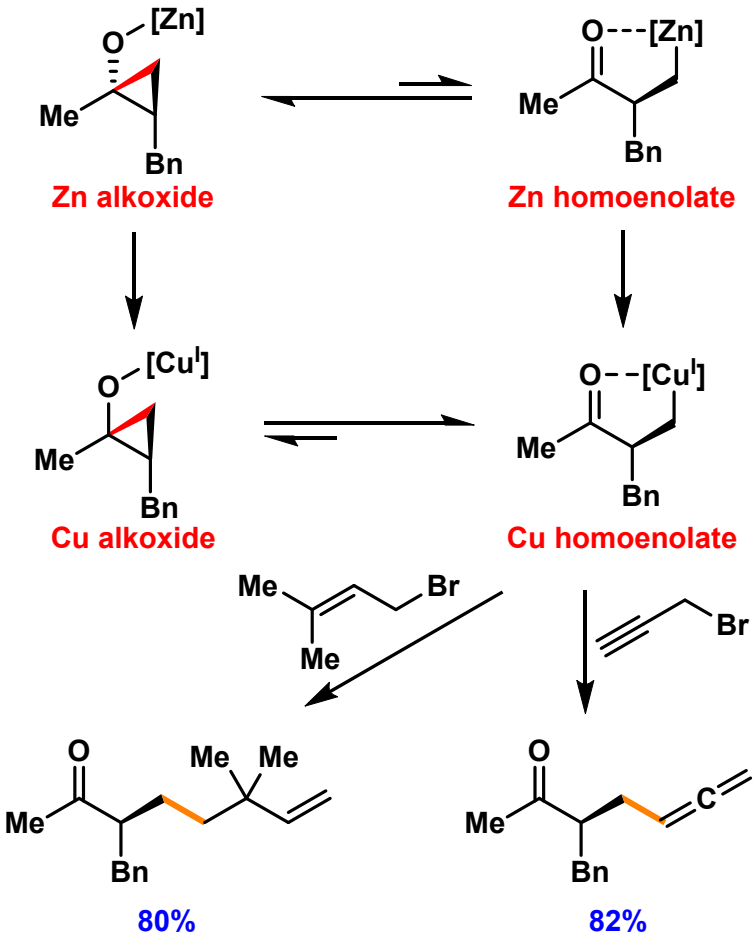


J. Am. Chem. Soc. **1987**, *109*, 8056.





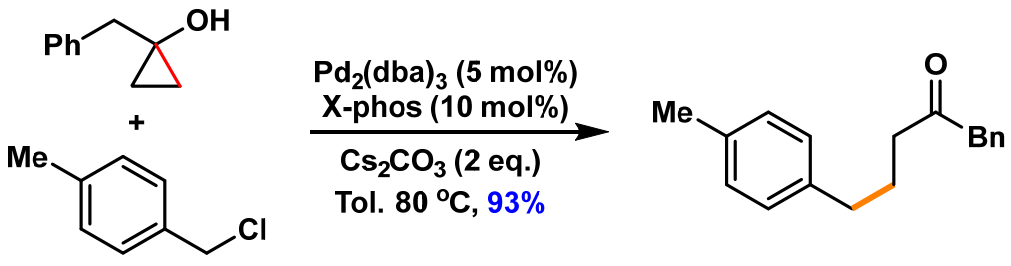
Chem. Lett. **2007**, *36*, 164.

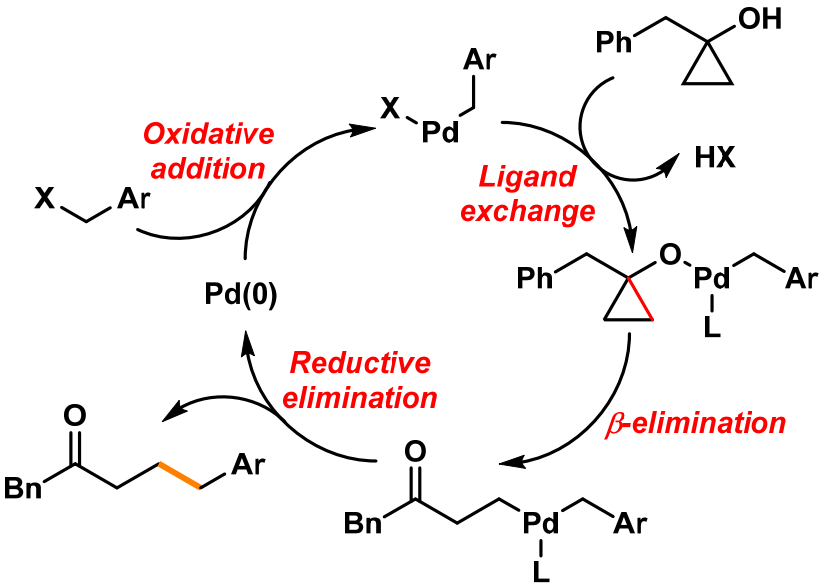


Angew. Chem., Int. Ed. **2012**, *51*, 9517.

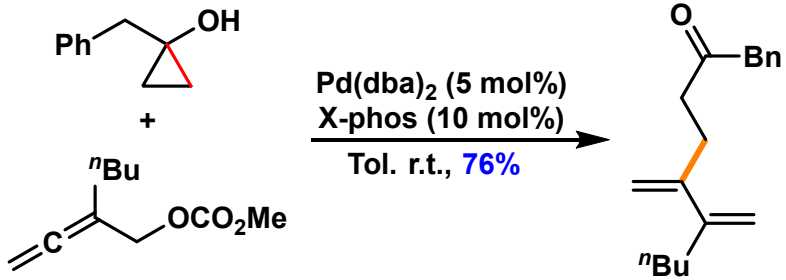
Metal Homoenolates

- β-Functionalization with C(sp^3)−X Electrophiles
  - Pd-Catalyzed



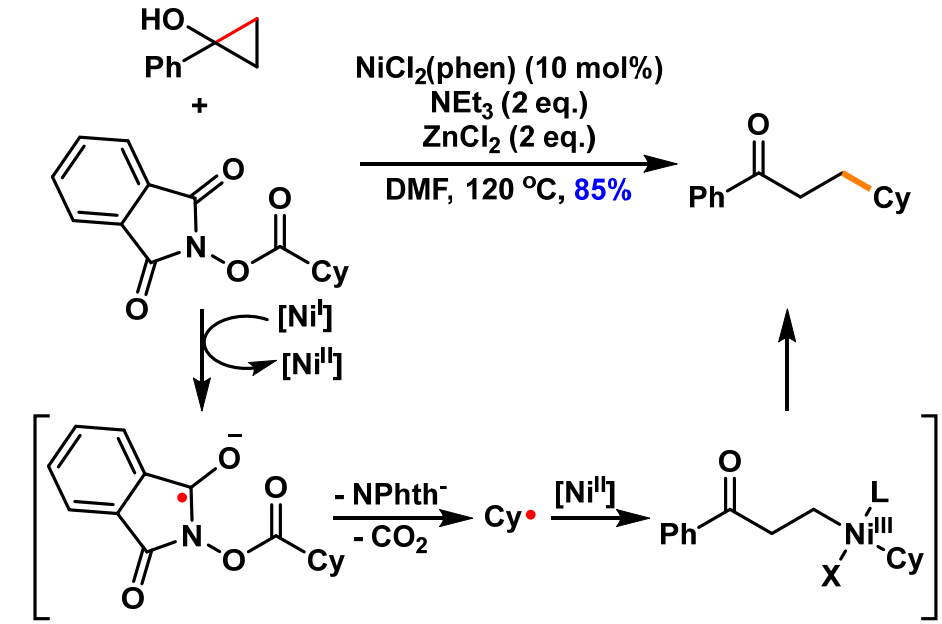


Org. Lett. **2014**, *16*, 5854.



Chem. Commun. **2019**, *55*, 4523.

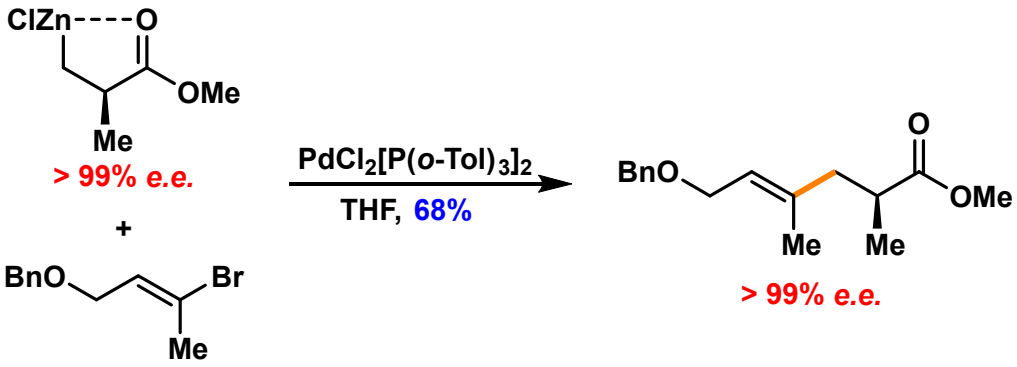
- Ni-Catalyzed



Org. Lett. **2019**, *21*, 8805.

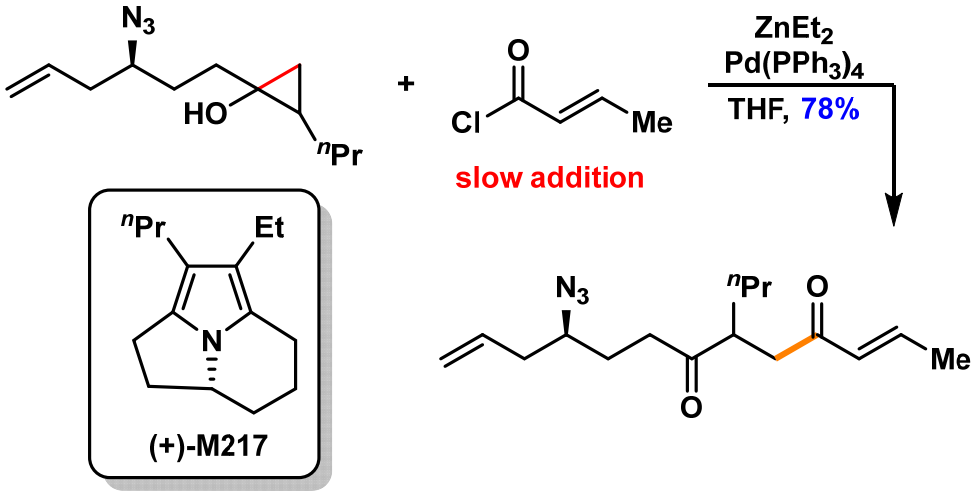
Metal Homoenolates

➢ β-Functionalization with C(sp^2)−X and C(sp)−X Electrophiles



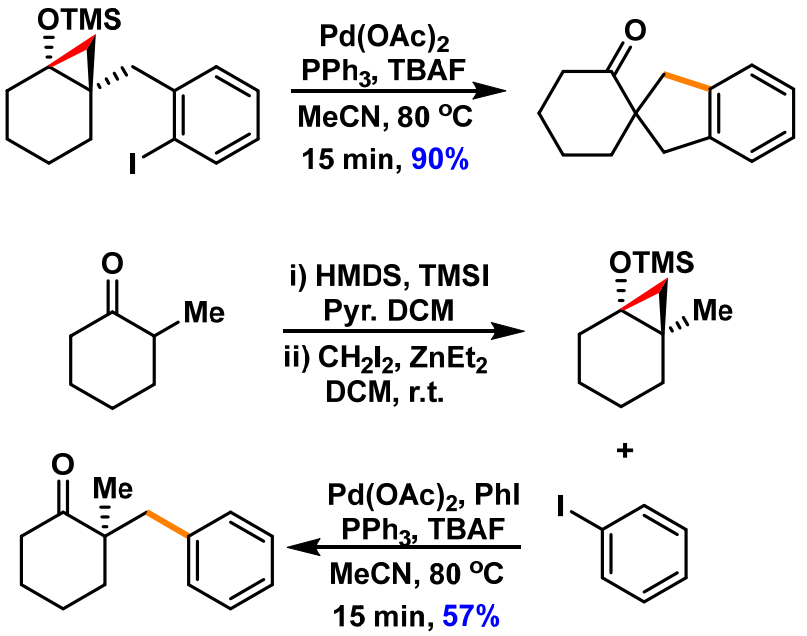
Org. Lett. **2004**, *6*, 2845.

➢ C-Acylation



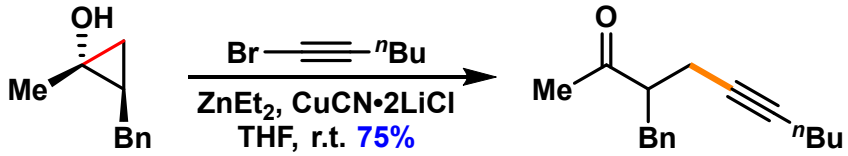
Org. Lett. **2013**, *15*, 1780.

➢ C-Arylated (TMS-protected)



Org. Lett. **2011**, *13*, 110.

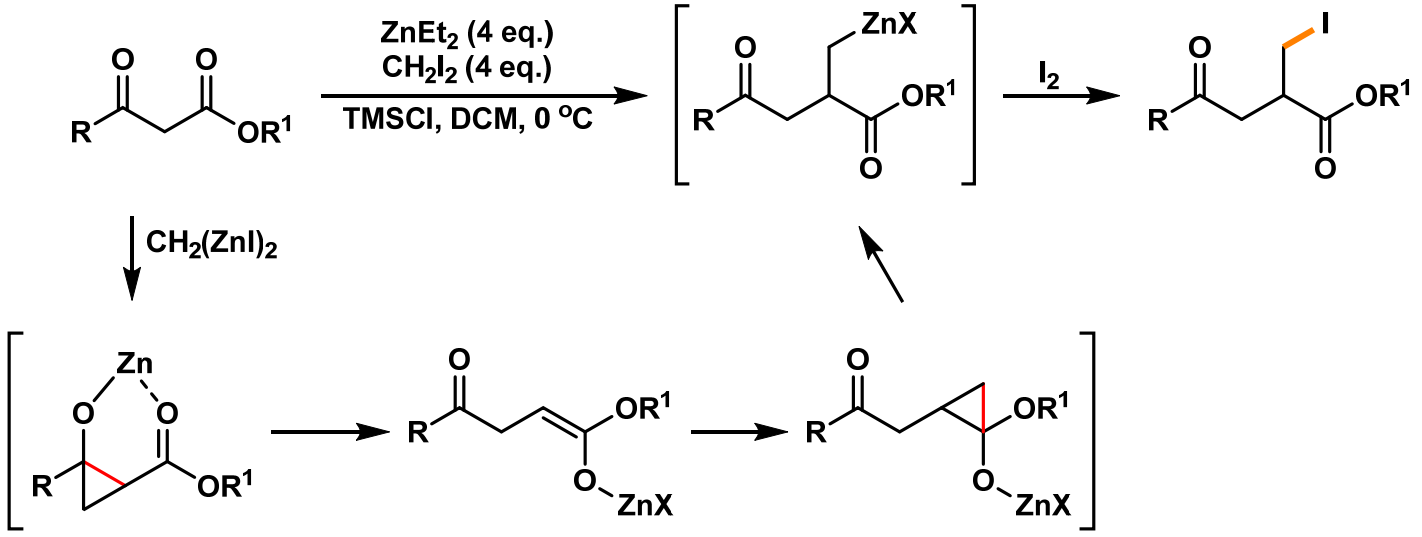
➢ β-Alkynylation



Org. Lett. **2015**, *17*, 3854.

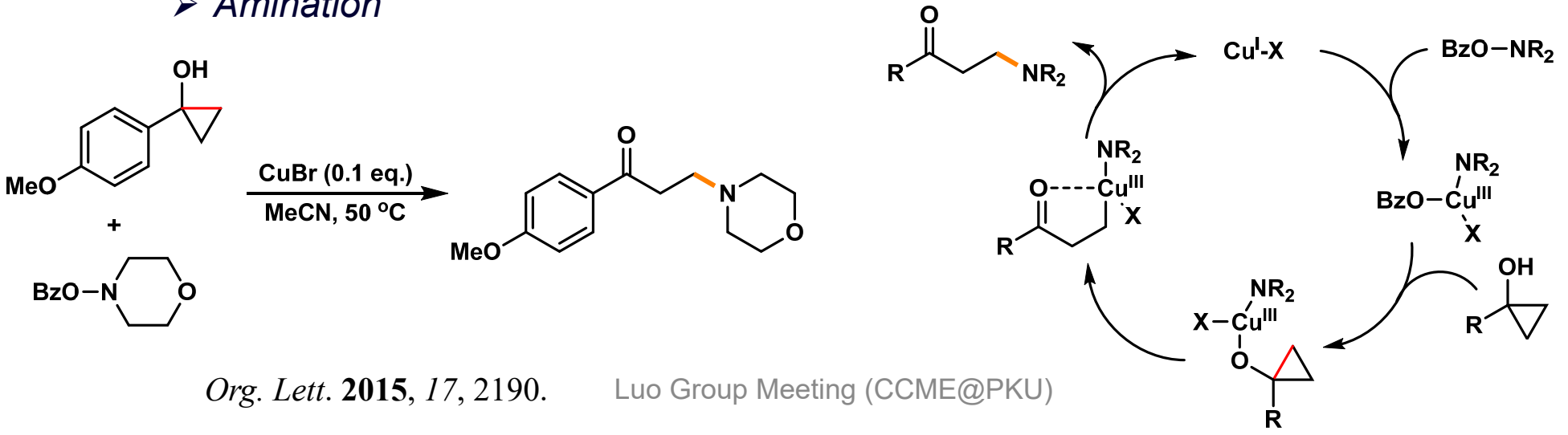
Metal Homoenolates

- *β-Functionalization with Heteroatom−X Electrophiles*
  - *Iodination*



Tetrahedron, **2008**, *64*, 8045.

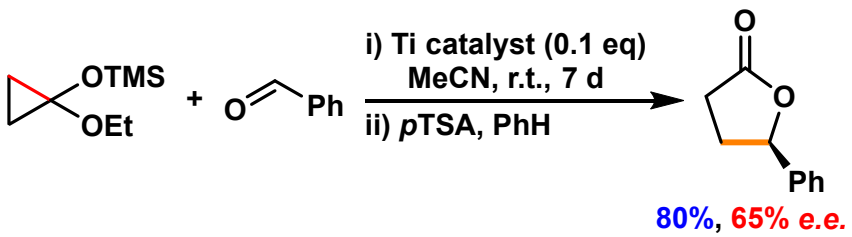
  - *Amination*



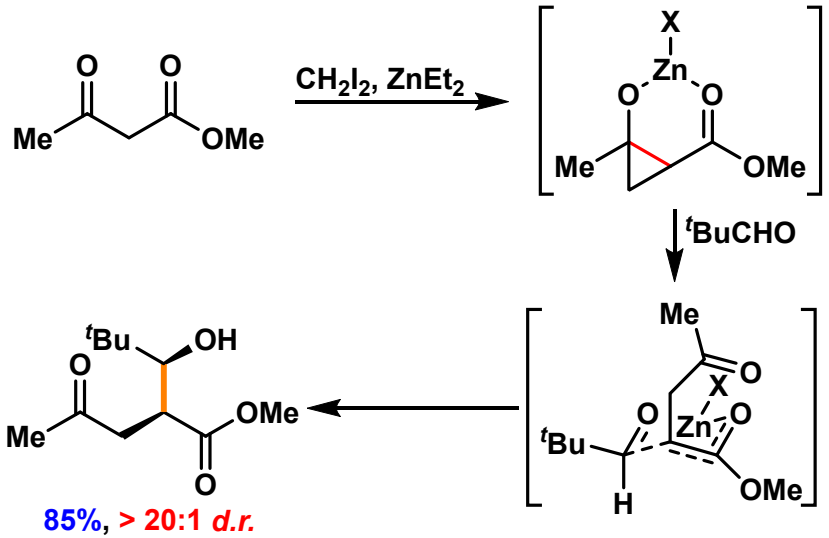
Org. Lett. **2015**, *17*, 2190.

Metal Homoenolates

- *β-Functionalization with π Electrophiles*
  - *Carbonyl Derivatives*

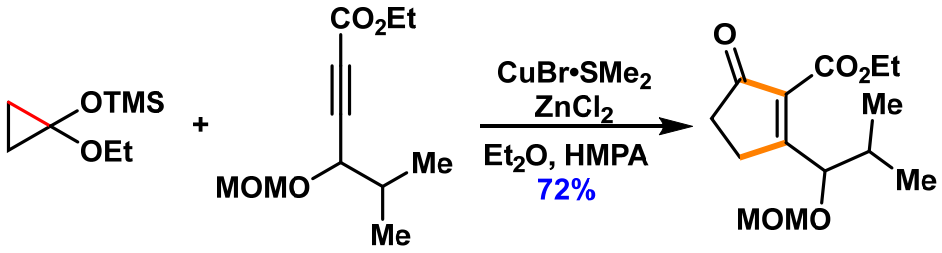


Synlett, **2003**, 390.

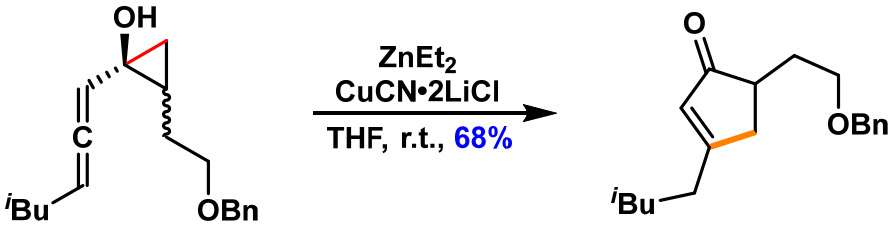


Org. Lett. **2001**, *3*, 4169.

- *Olefins ---- Formal [3+2]-cycloaddition*



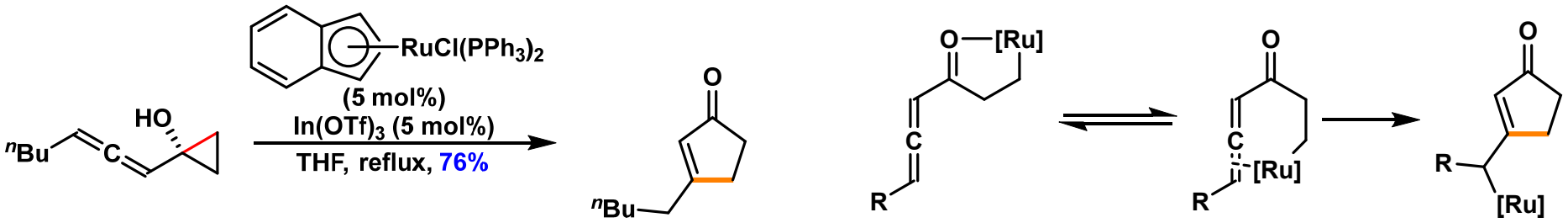
J. Org. Chem. **1990**, *55*, 4235.

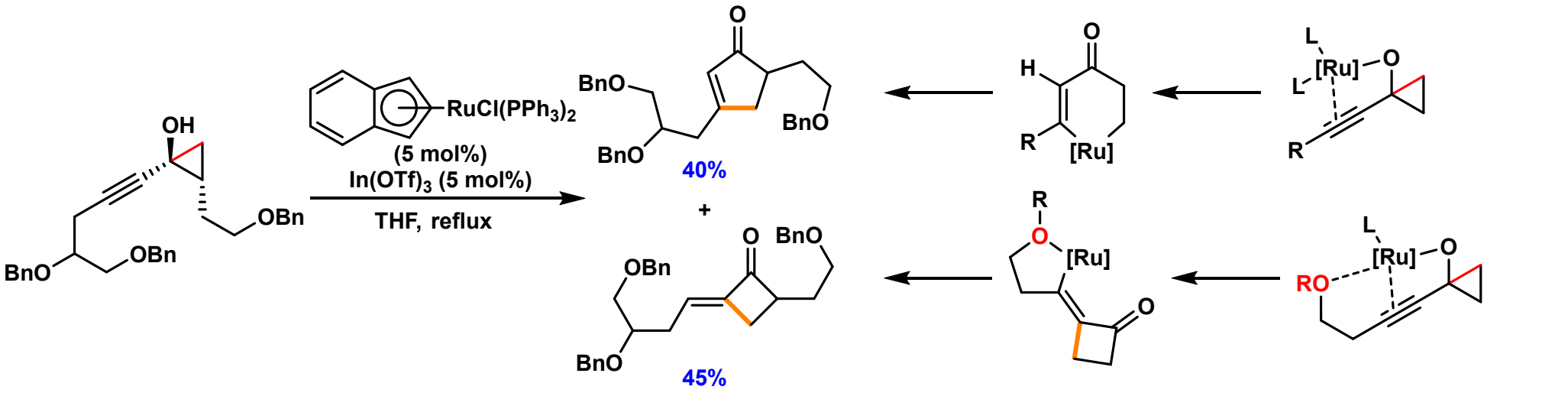


J. Org. Chem. **2017**, *82*, 4379.

Metal Homoenolates

- *β-Functionalization with π Electrophiles*
  - *Olefins ---- Formal [3+2]-cycloaddition*



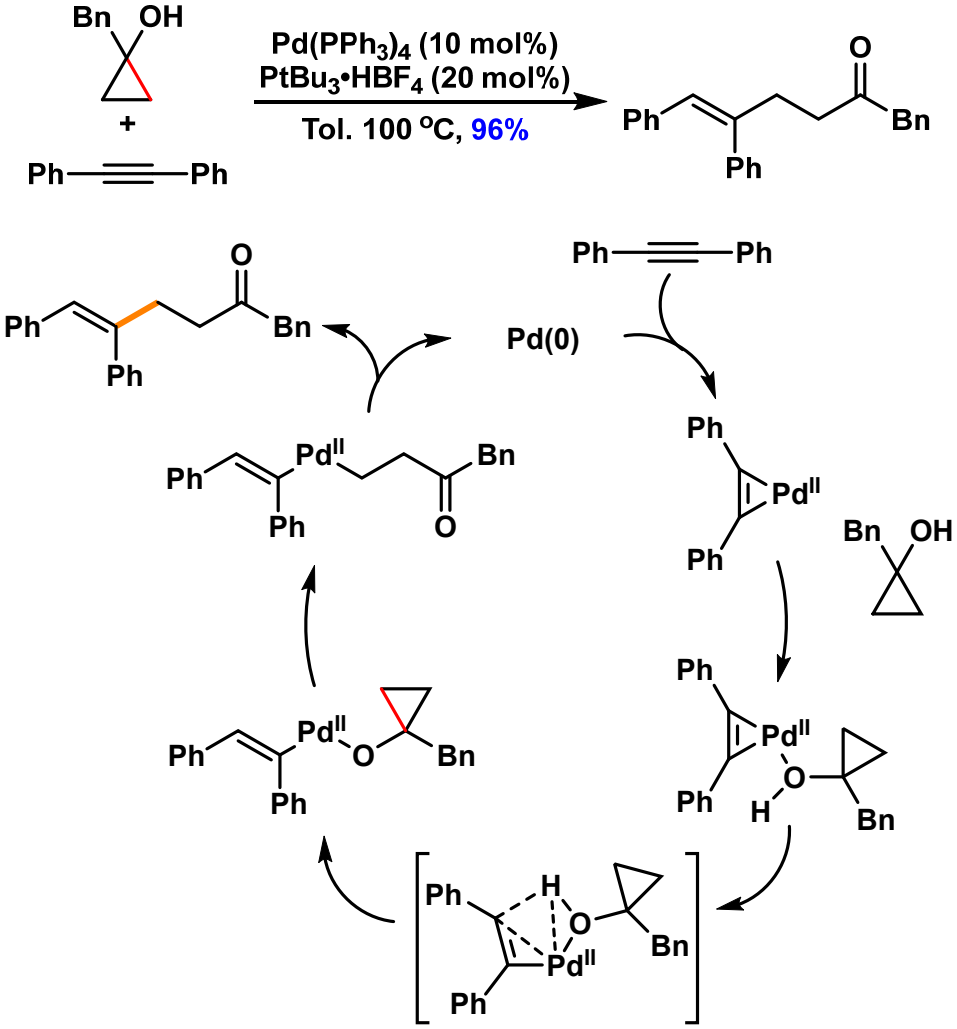


Org. Lett. 2016, *18*, 5098.

Metal Homoenolates

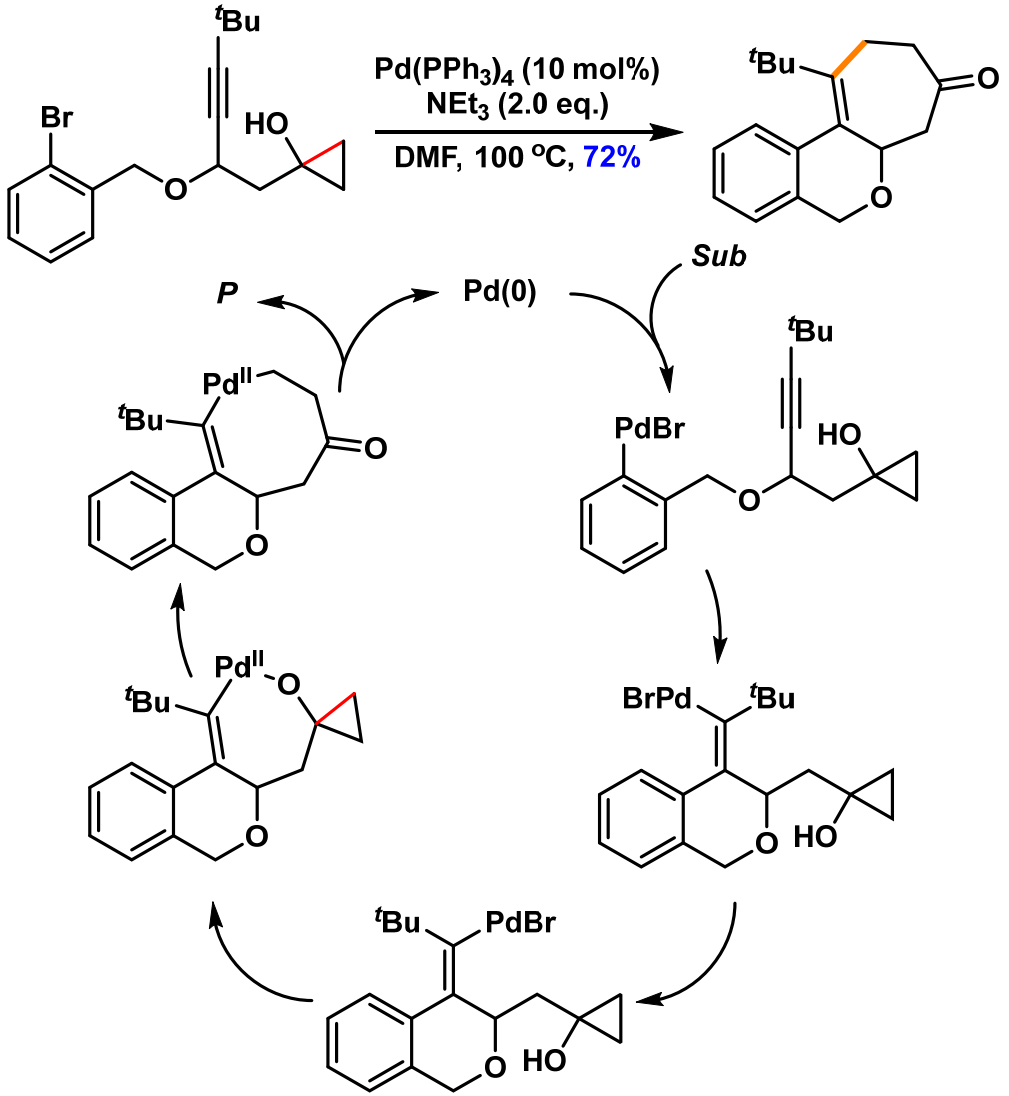
➢ β-Functionalization with π Electrophiles

➢ Alkynes



Adv. Synth. Catal. **2018**, *360*, 3171.

➢ Difunctionalization

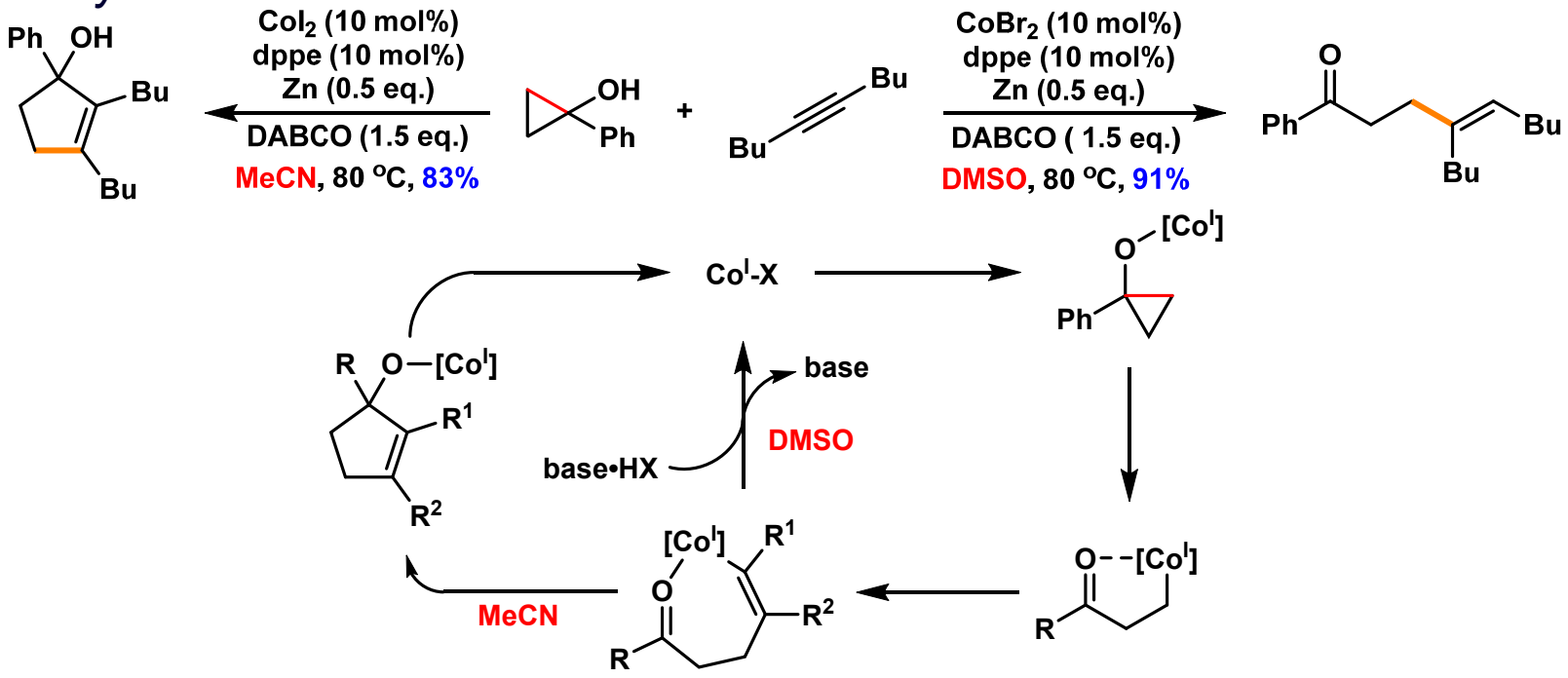


Org. Lett. **2018**, *20*, 7266.

Metal Homoenolates

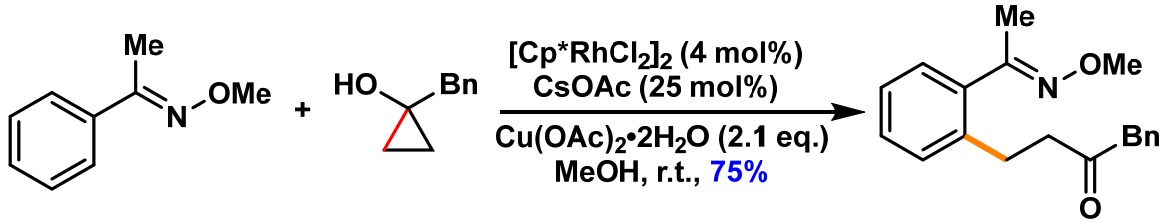
➢ β-Functionalization with π Electrophiles

➢ Alkynes

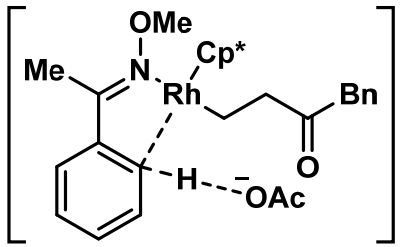


Chem. Sci. **2018**, *9*, 6928.

➢ Arenes



ACS Catal. **2016**, *6*, 647.

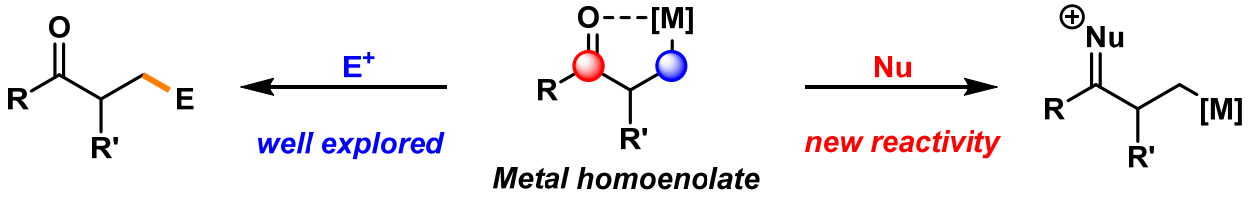


Outer-sphere CMD
Rate-determining Step

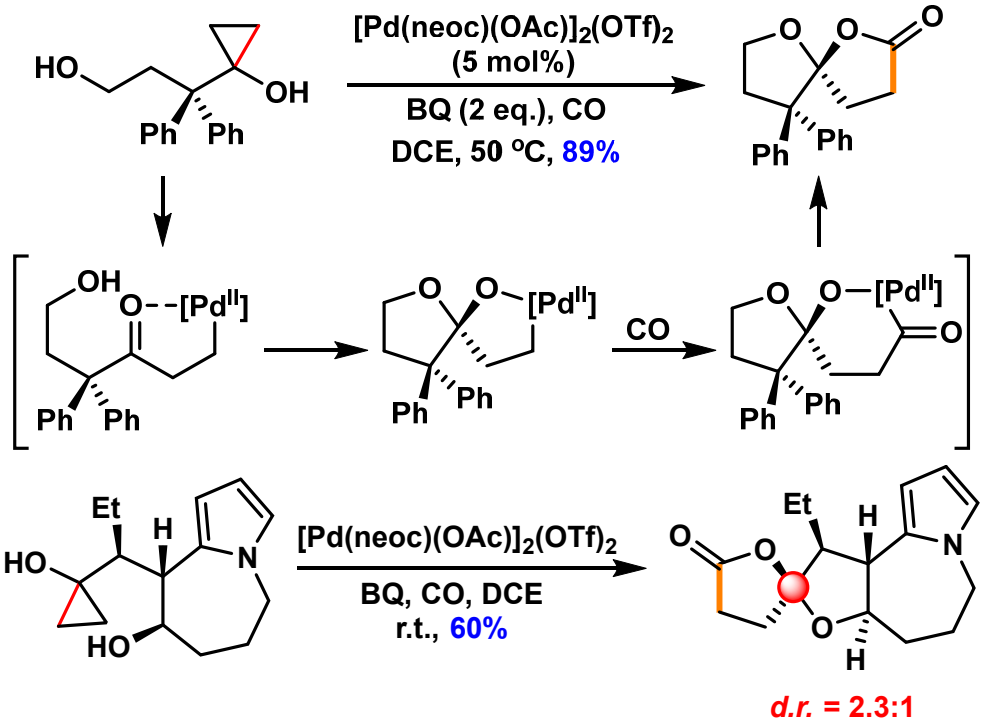
J. Org. Chem. **2019**, *84*, 11150.

Metal Homoenolates

➢ β-Functionalization of Cyclopropyl Alcohols with Nucleophiles

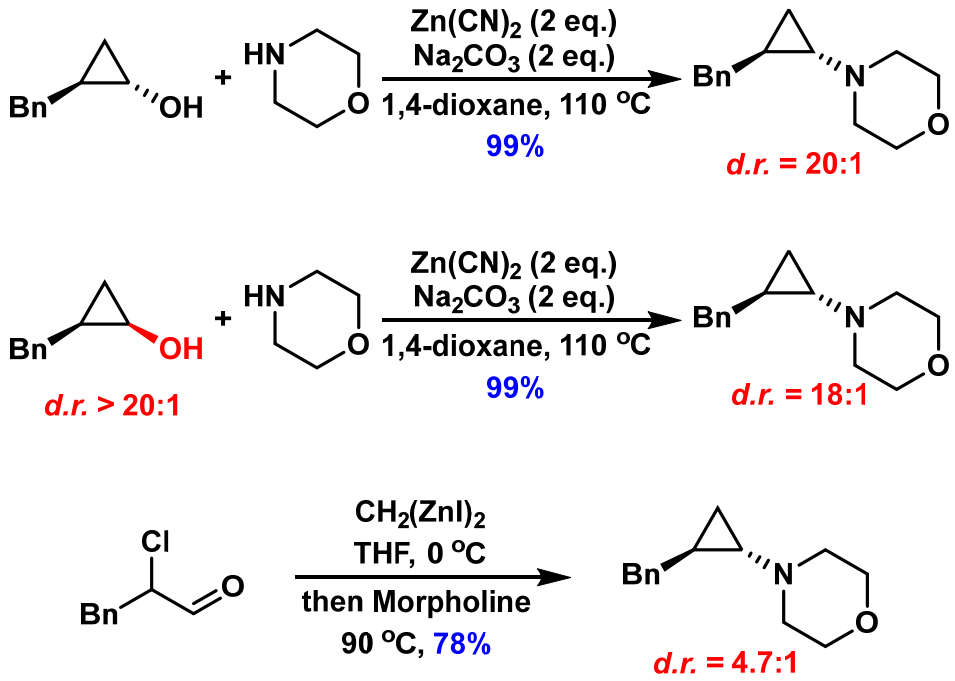


➢ Pd-Catalyzed Spirolactonization



J. Am. Chem. Soc. **2016**, *138*, 10693.
Angew. Chem. Int. Ed. **2018**, *57*, 15209.

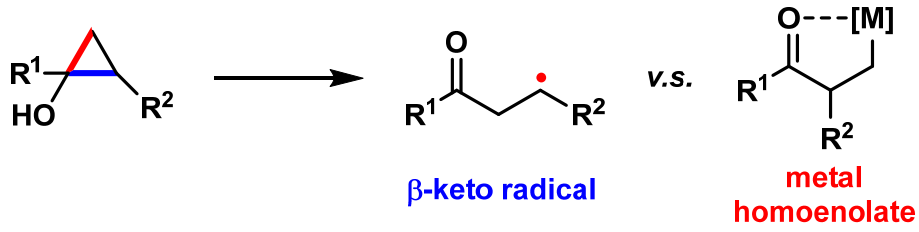
➢ Synthesis of Cyclopropylamnies



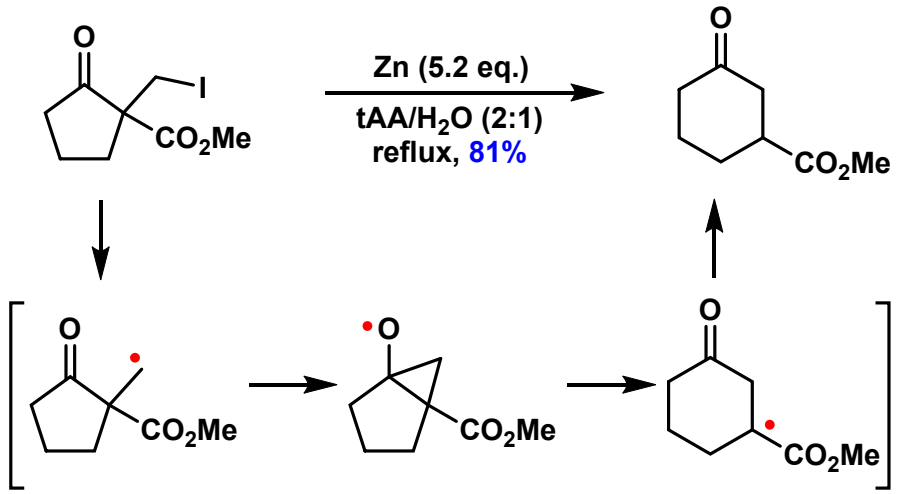
J. Am. Chem. Soc. **2017**, *139*, 11357.

β-keto Radicals

- *Radical Versus Anionic Pathways*

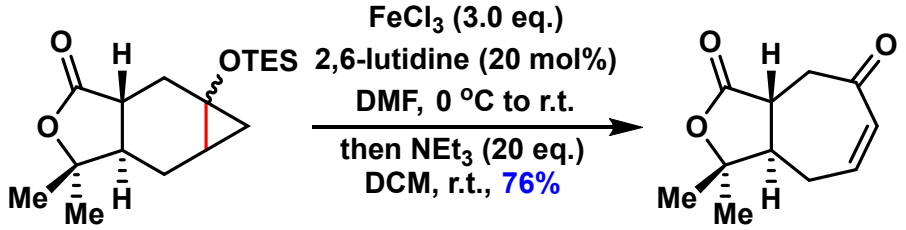


- *Homologations*
  - *Reductive condition*

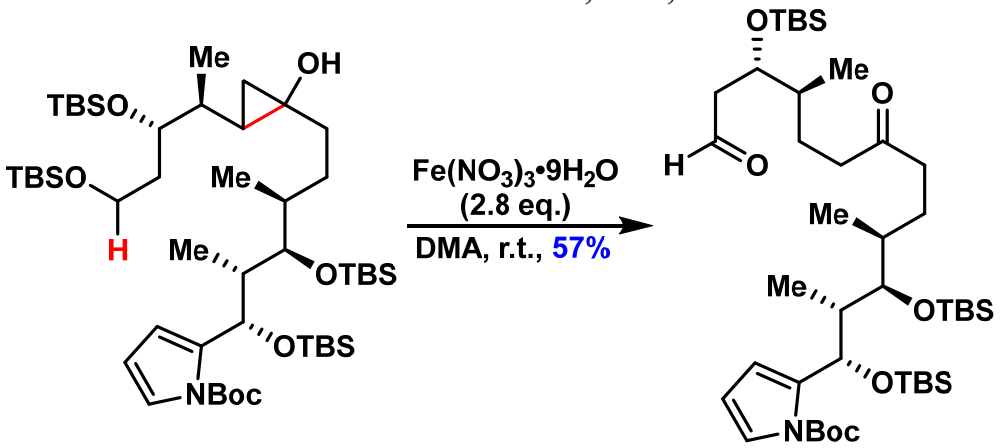


J. Org. Chem. **2003**, *68*, 7629.

- *Oxidative condition*



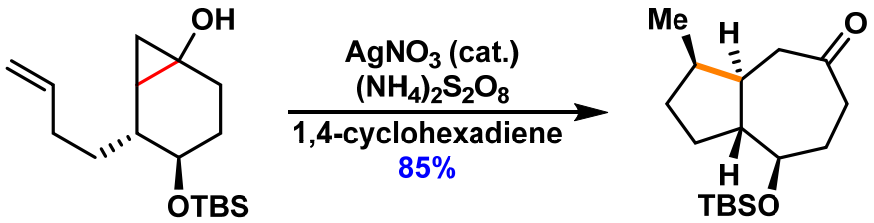
J. Am. Chem. Soc. **2020**, *142*, 573.



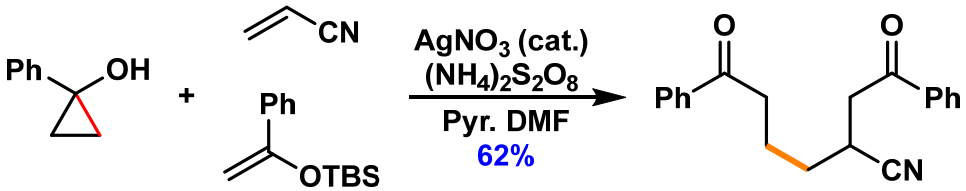
Chem. - Asian J. **2013**, *8*, 2792.

β-keto Radicals

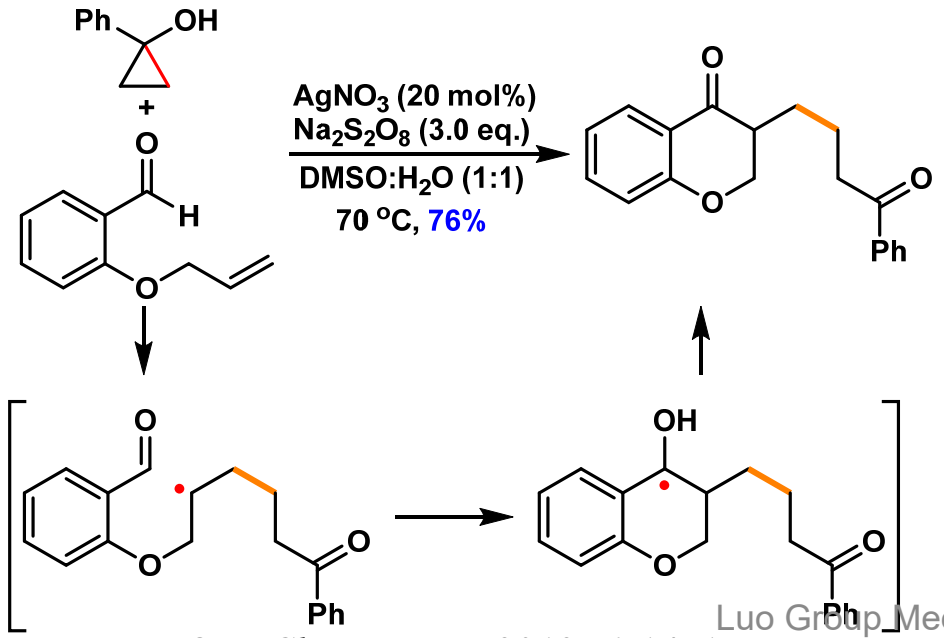
➢ Additions to Unsaturated Systems



Chem. Lett. **2004**, *33*, 942.

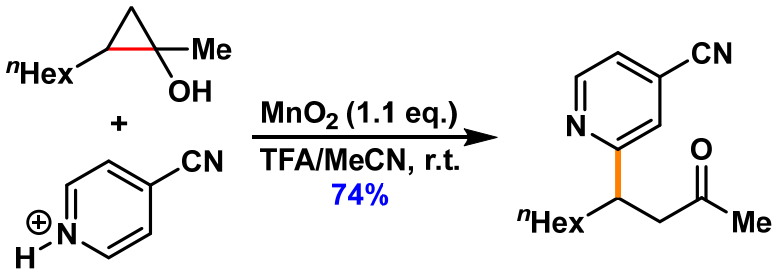


Chem. Lett. **2006**, *35*, 18.



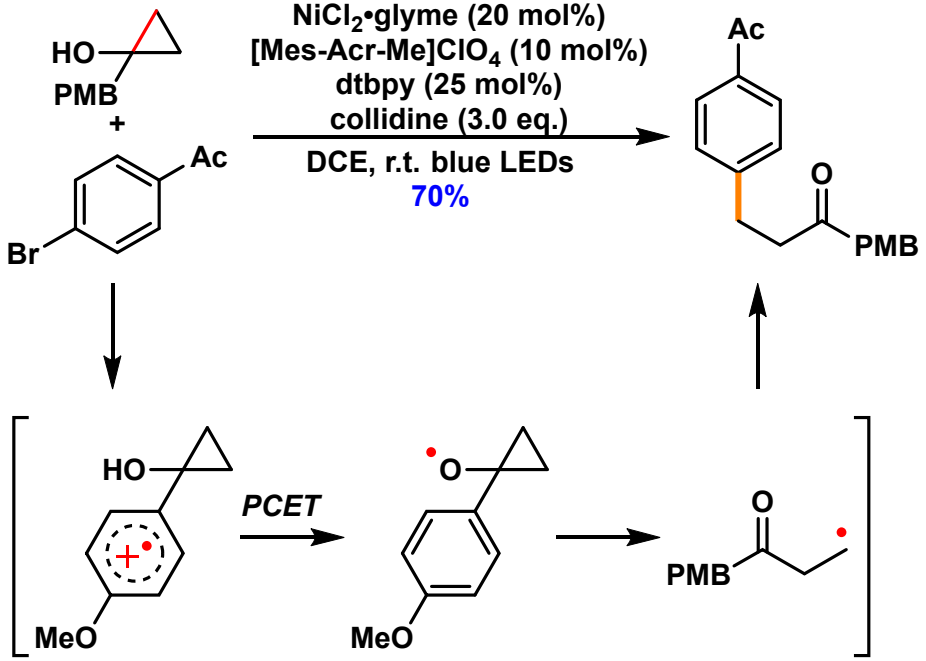
Org. Chem. Front. **2019**, *6*, 1471.

➢ Minisci-type reaction



Eur. J. Org. Chem. **2016**, 26.

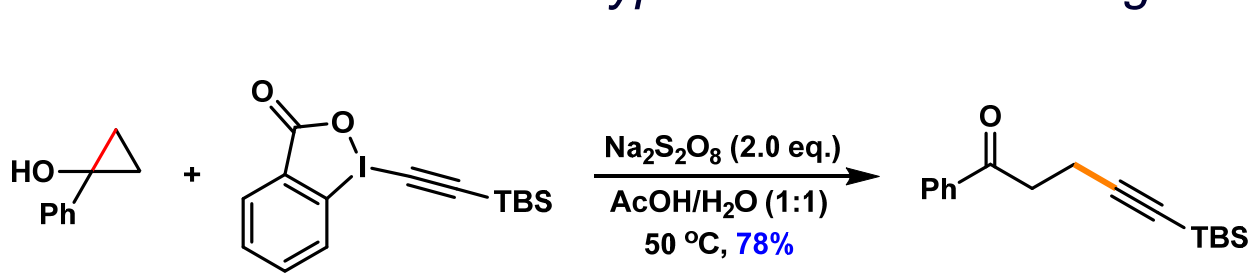
➢ Cross-coupling reaction

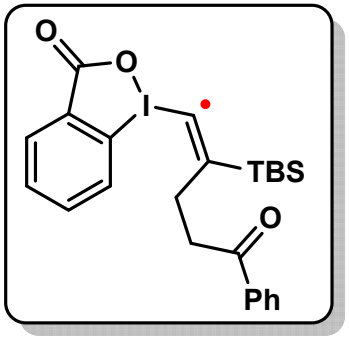


J. Am. Chem. Soc. **2020**, *142*, 3532.

β-keto Radicals

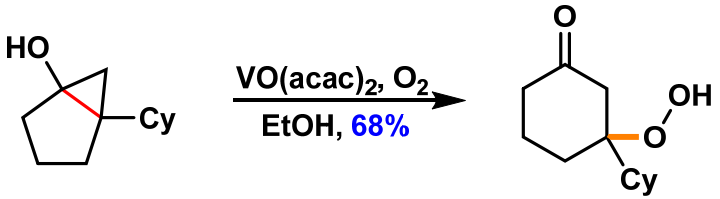
➢ C-C Bond Formation via Hypervalent Iodine Reagents



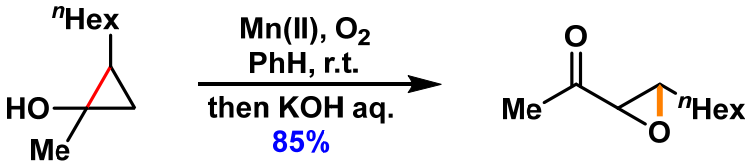


Org. Lett. **2015**, *17*, 4798.

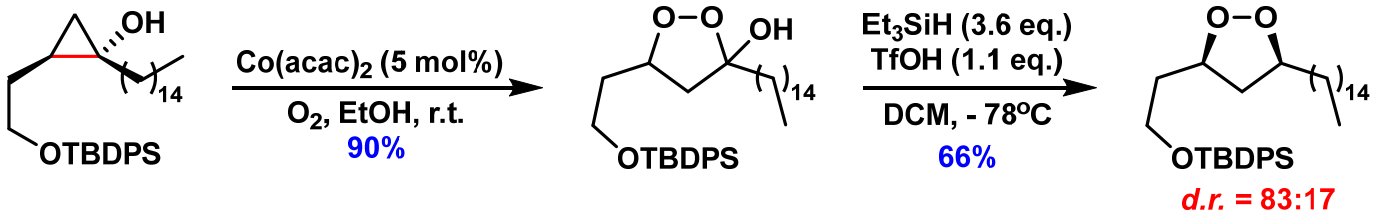
➢ Peroxide and Epoxide Formation



Tetrahedron Lett. **1999**, *40*, 4045.



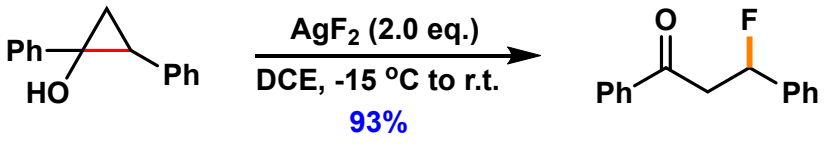
Synthesis, **2001**, *10*, 1453.



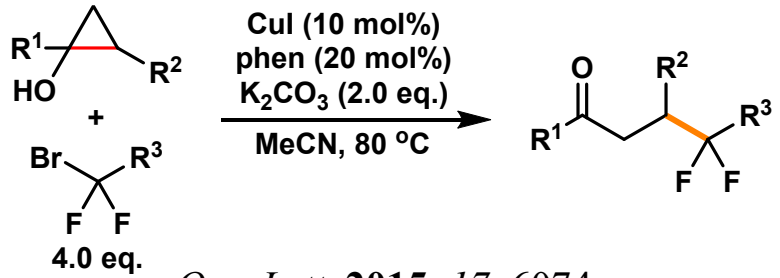
Tetrahedron Lett. **2016**, *57*, 5286.

β-keto Radicals

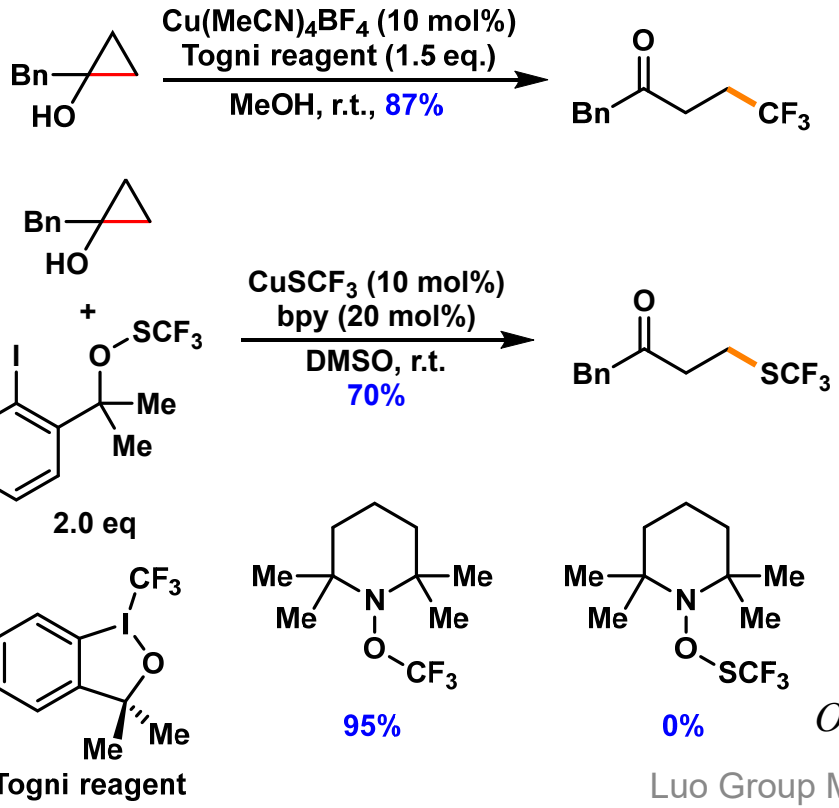
➢ Fluorinated Functional Groups



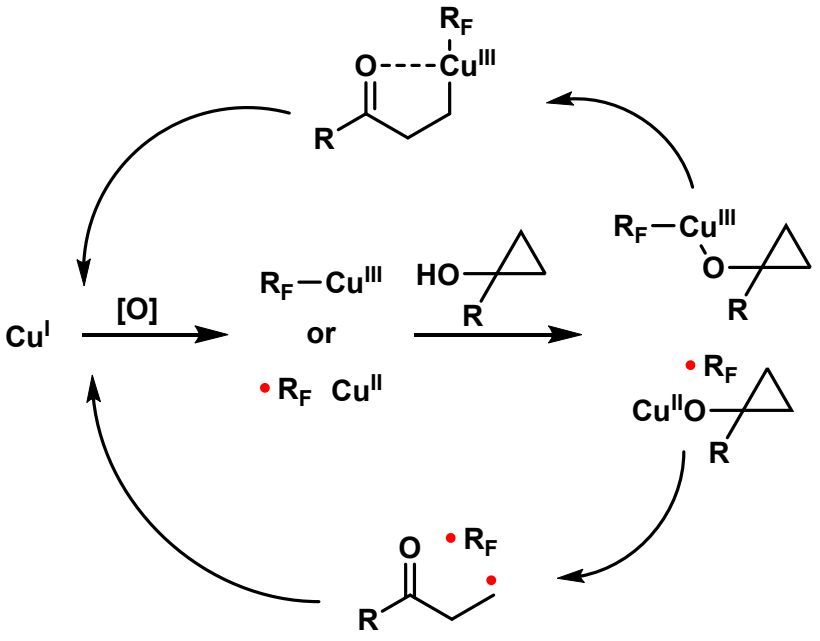
Eur. J. Org. Chem. **2017**, 5872.



Org. Lett. **2015**, *17*, 6074.



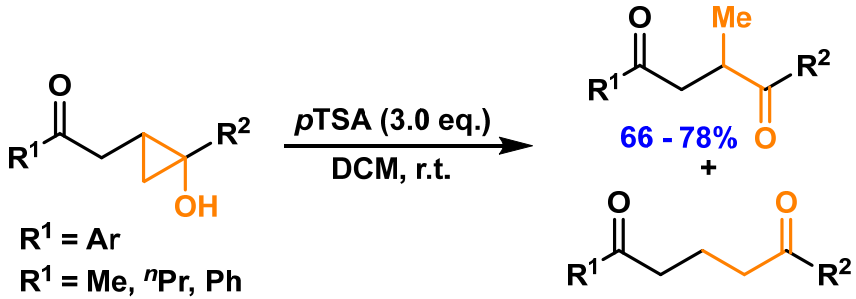
➢ Proposed Mechanism



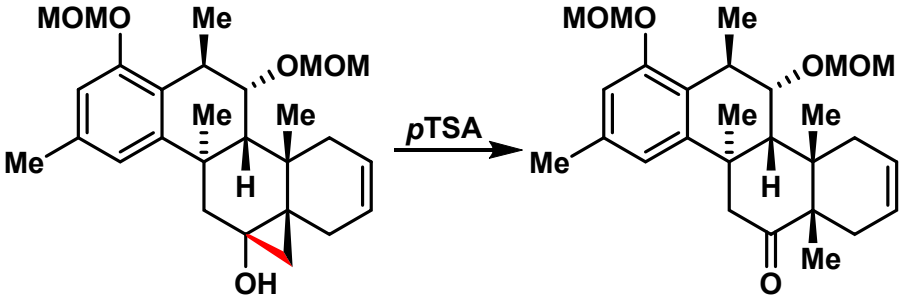
Org. Lett. **2015**, *17*, 2186.

Acid-Mediated Ring Opening

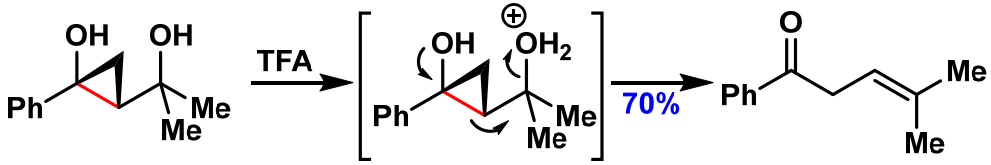
➢ Ring Opening with Brønsted Acid



Tetrahedron, **2006**, *62*, 7762.



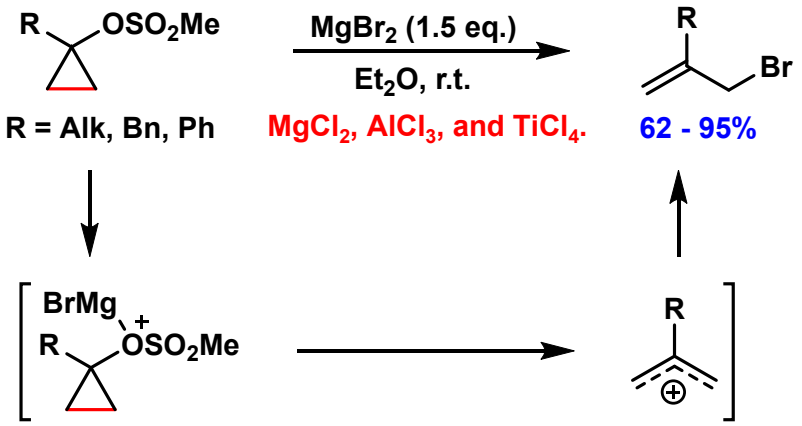
Chem. - Asian J. **2008**, *3*, 1549.



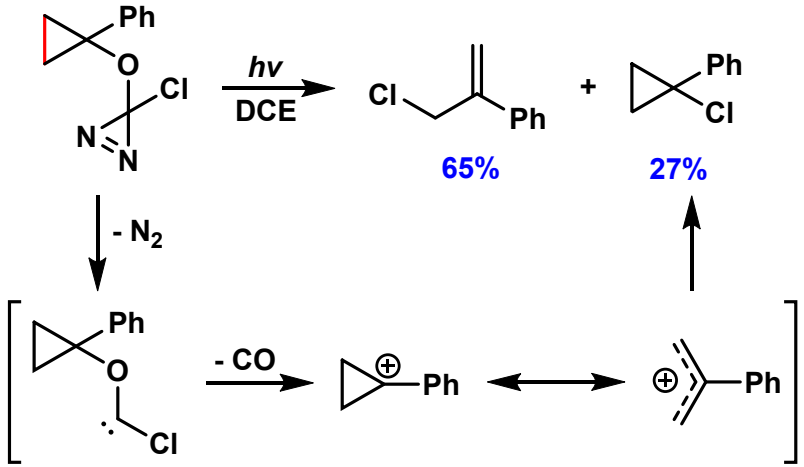
Synlett, **2008**, 1412.

➢ Ring Opening with Lewis Acid

➢ Via Cation-Allyl Isomerization



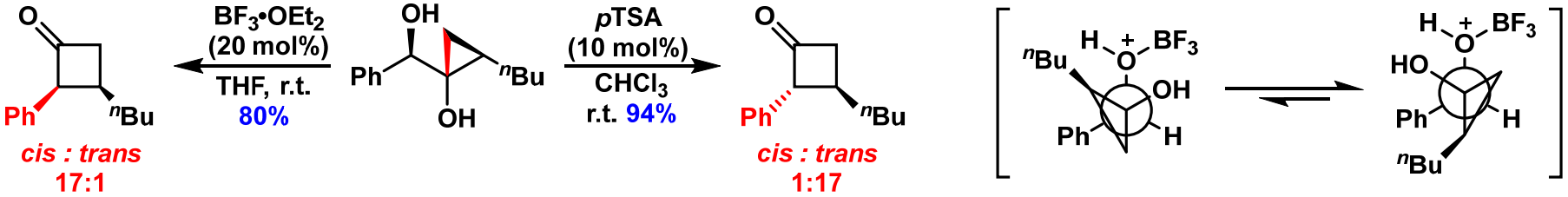
Synlett, **2002**, 443.



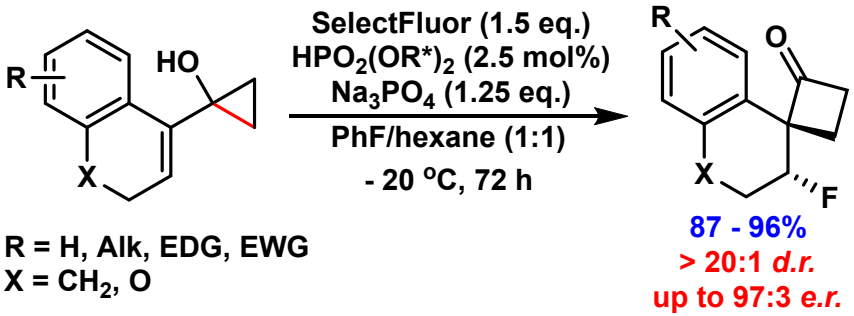
Tetrahedron Lett. **2004**, *45*, 3321.

Acid-Mediated Ring Opening

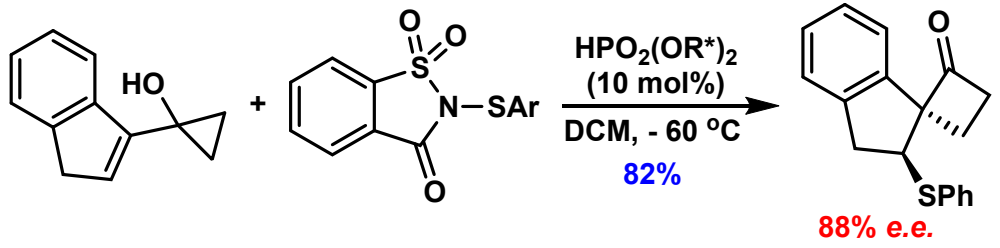
- *Formation of 4 Membered Ring via Intramolecular Cyclization*
  - *Pinacol-type Rearrangement*



J. Am. Chem. Soc. **2009**, *131*, 6516.

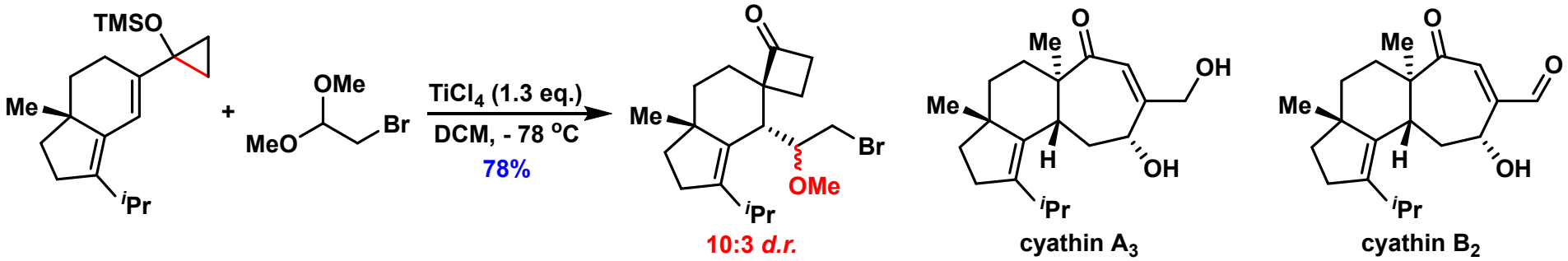


Angew. Chem. Int. Ed. **2013**, *52*, 9266.



Angew. Chem. Int. Ed. **2019**, *58*, 12491.

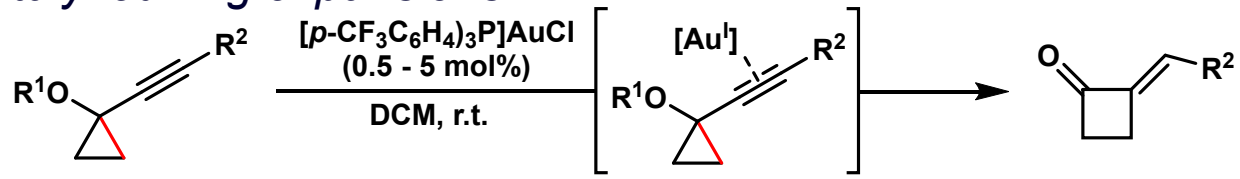
  - *Vinylogous Mukaiyama condensation*



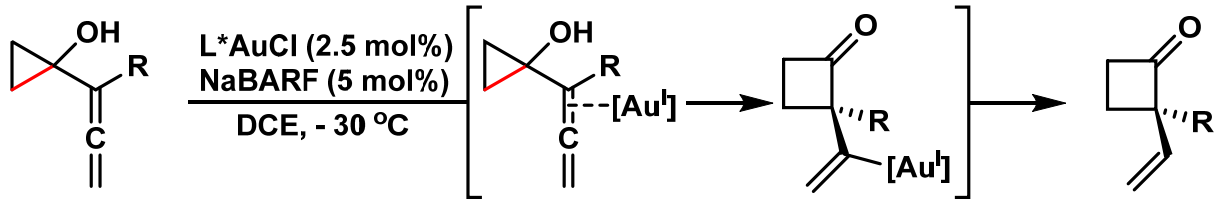
Angew. Chem. Int. Ed. **2009**, *48*, 5334.

Acid-Mediated Ring Opening

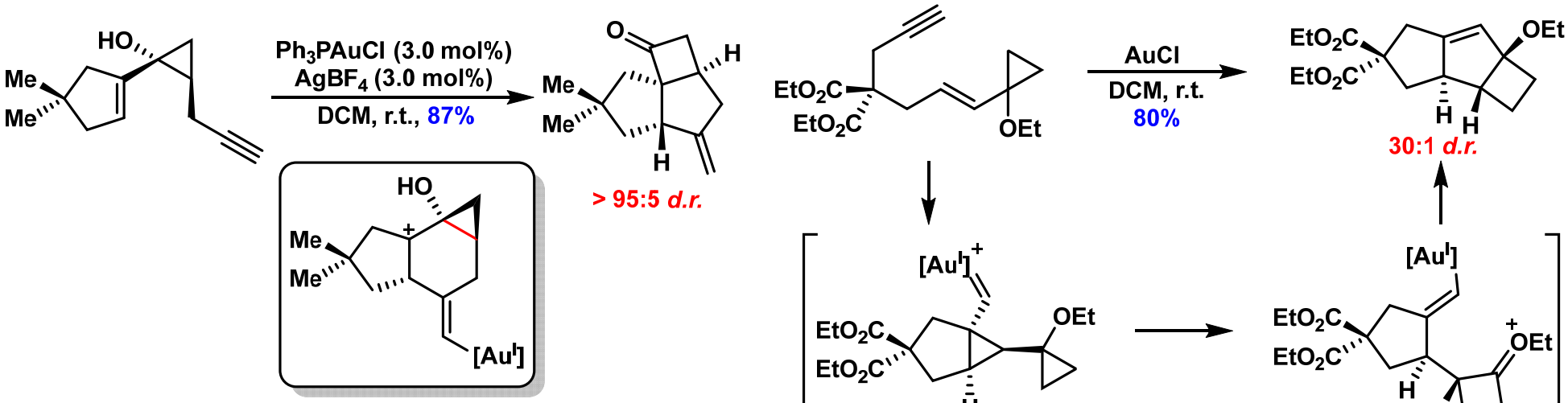
- *Formation of 4 Membered Ring via Intramolecular Cyclization*
  - *Gold-catalyzed ring expansions*



J. Am. Chem. Soc. **2005**, *127*, 9708.



J. Am. Chem. Soc. **2009**, *131*, 9178.

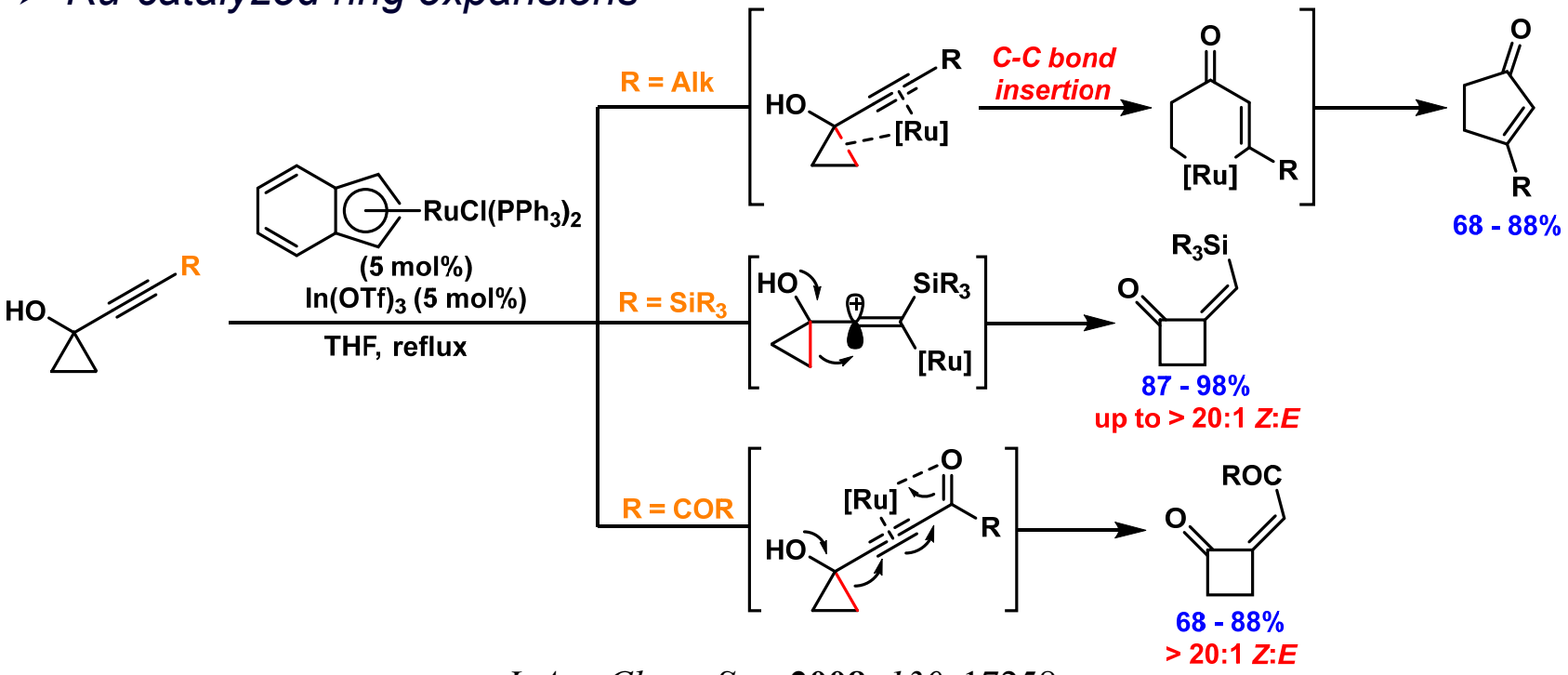


Org. Lett. **2008**, *10*, 4315.

Angew. Chem. Int. Ed. **2006**, *45*, 5452.

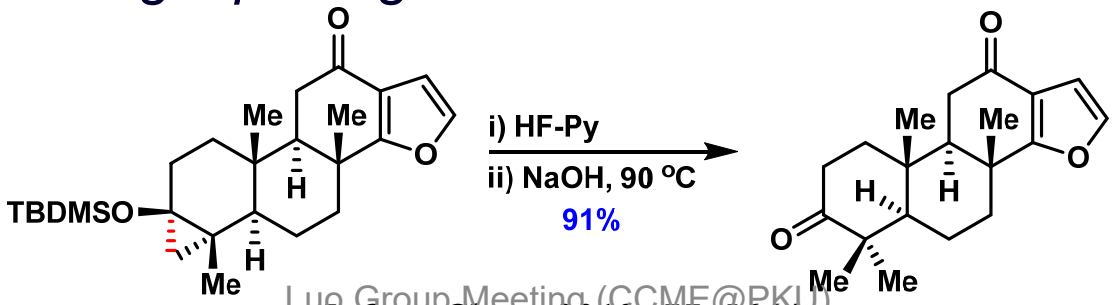
Acid-Mediated Ring Opening

- *Formation of 4-5 Membered Ring via Intramolecular Cyclization*
  - *Ru-catalyzed ring expansions*



J. Am. Chem. Soc. **2008**, *130*, 17258.

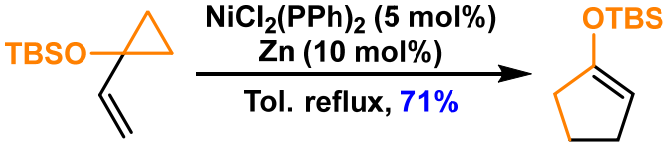
- *Base-Mediated Ring Opening*

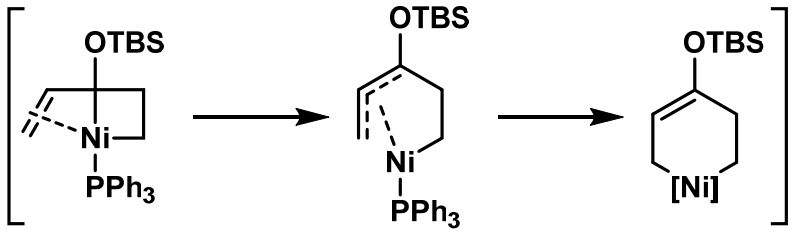


J. Org. Chem. **2012**, *77*, 5664.

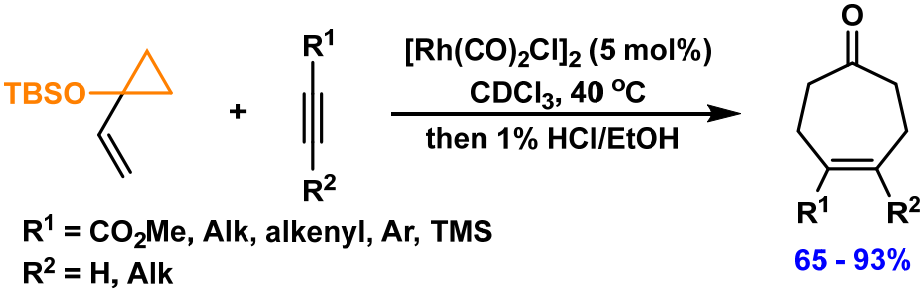
Metal-catalyzed C-C Insertions

➢ VCP isomerization

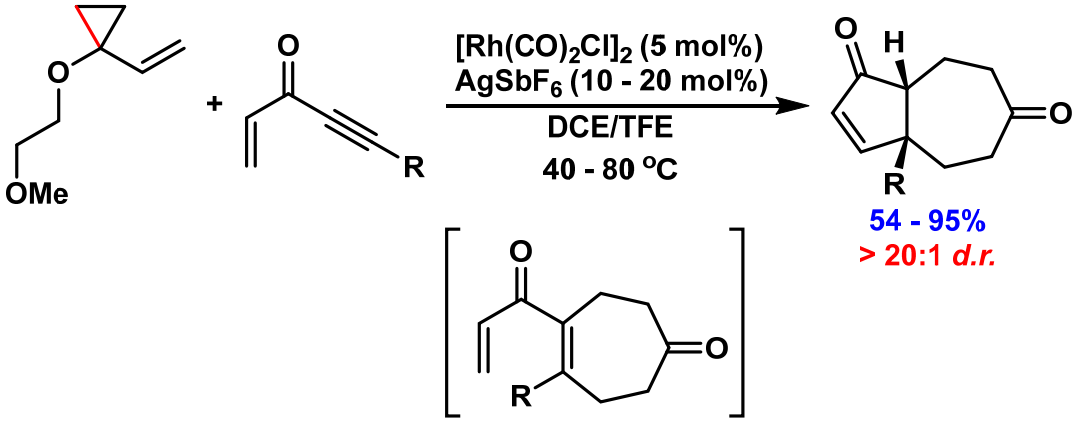




Synlett, **1994**, 941.

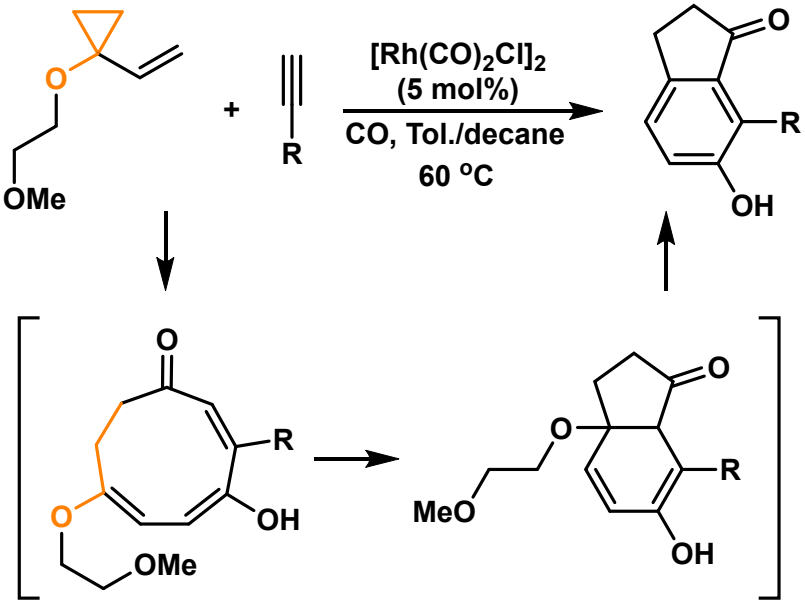


J. Am. Chem. Soc. **1998**, *120*, 10976.



J. Am. Chem. Soc. **2010**, *132*, 2532.

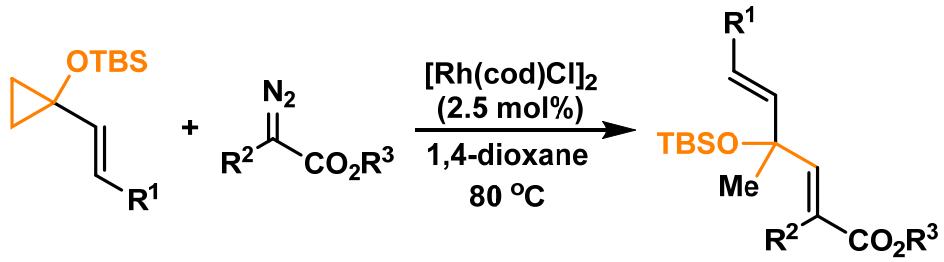
➢ Four-component [5+1+2+1]

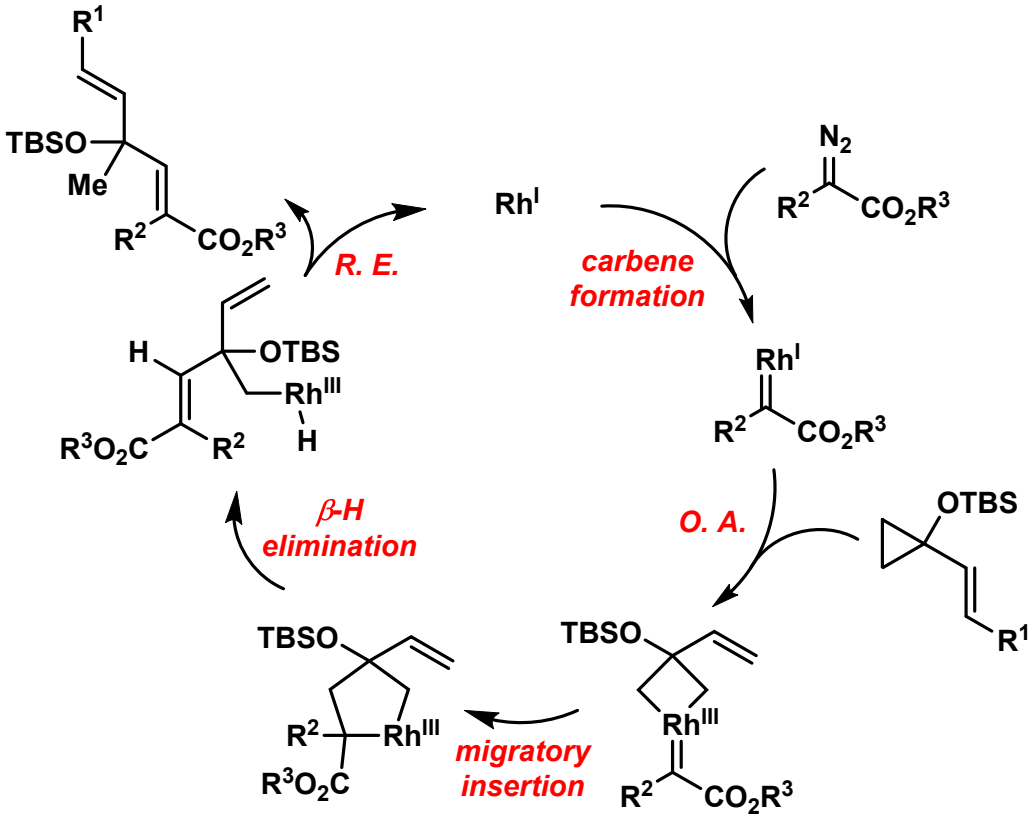


J. Am. Chem. Soc. **2005**, *127*, 2836.

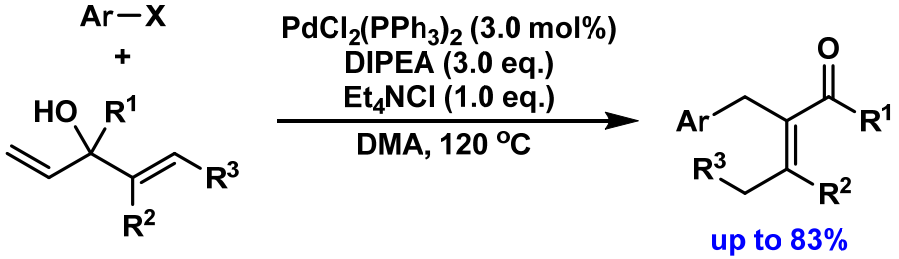
Metal-catalyzed C-C Insertions

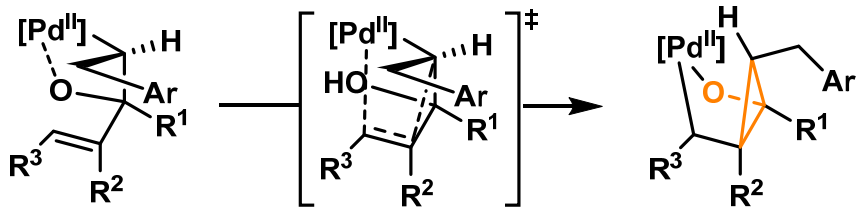
➢ Rh-catalyzed

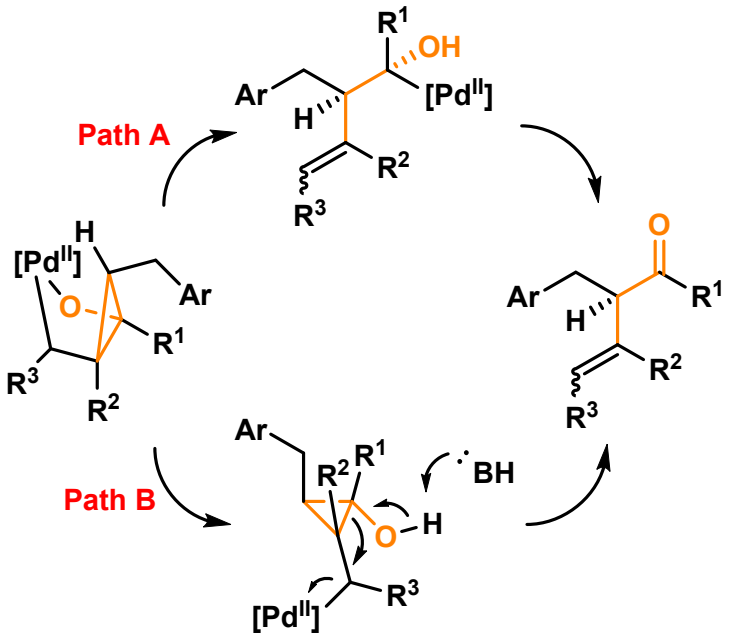




➢ Pd-catalyzed





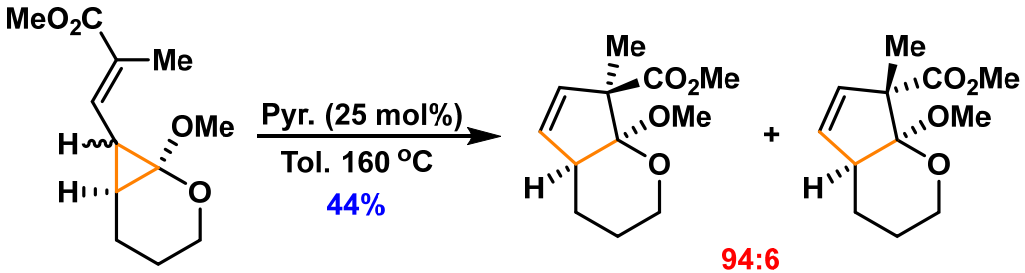


Angew. Chem. Int. Ed. **2016**, *55*, 15401.

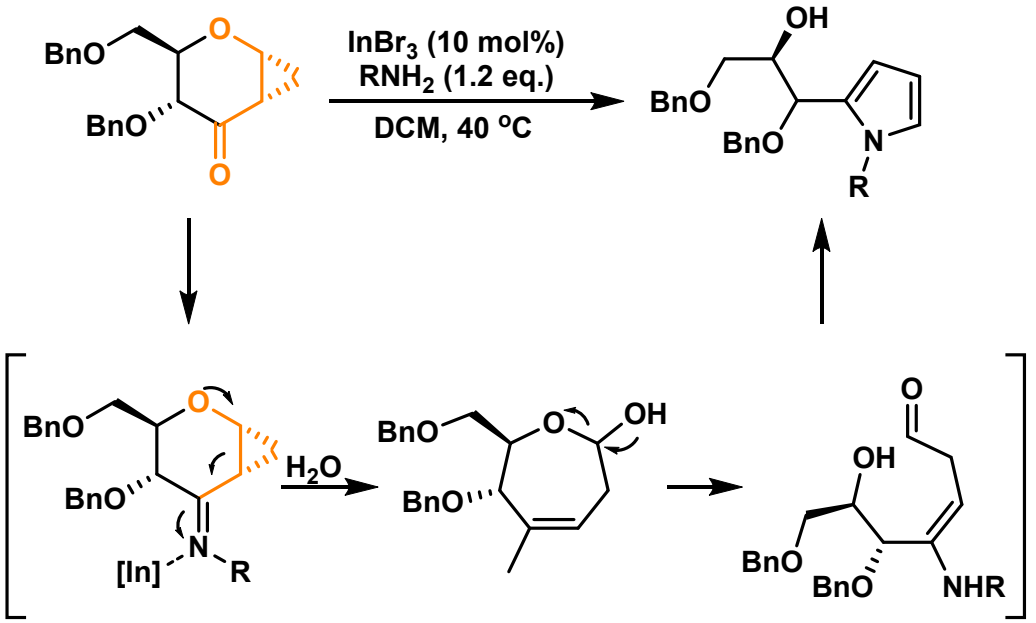
Org. Lett. **2005**, *7*, 5845.

Donor-Acceptor Chemistry

➢ Ring Opening Rearrangements

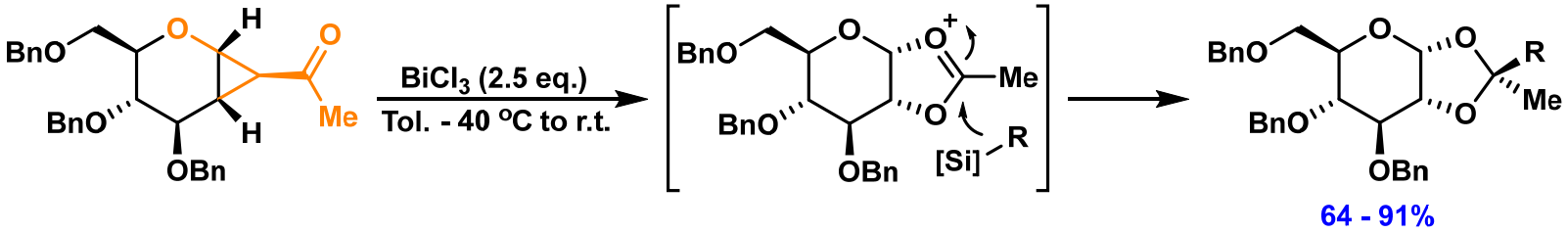


J. Am. Chem. Soc. **2012**, *134*, 5938.



Org. Lett. **2013**, *15*, 3852.

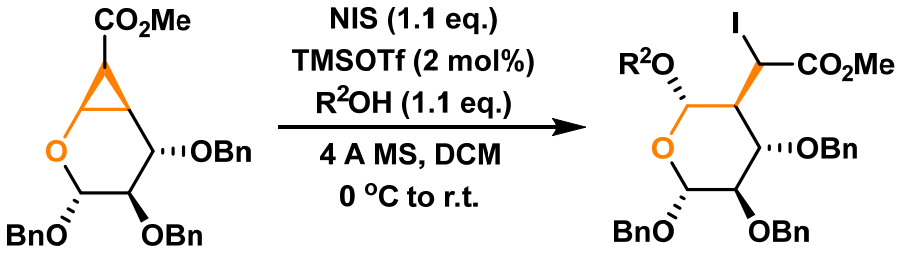
➢ Nucleophilic Addition to Donor-Acceptor Cyclopropanols



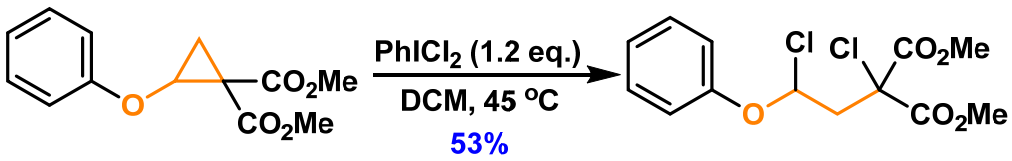
Chem. Commun. **2013**, *49*, 7085.

Donor-Acceptor Chemistry

➢ Difunctionalizations

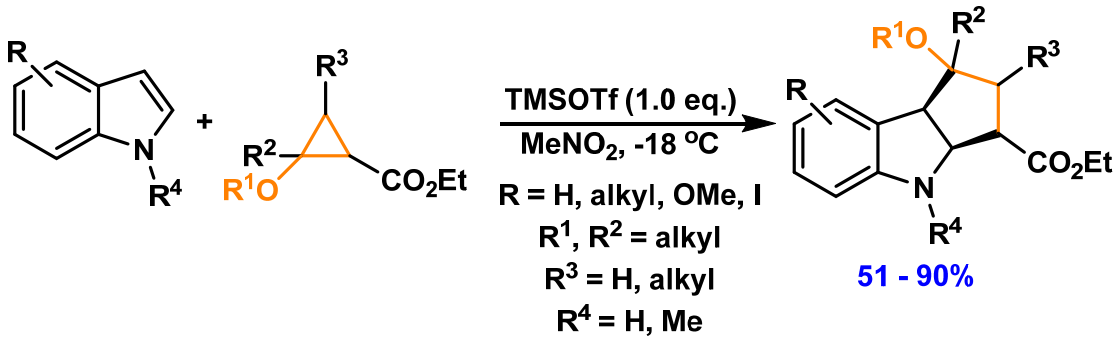


Chem. - Eur. J. **2009**, *15*, 7526.



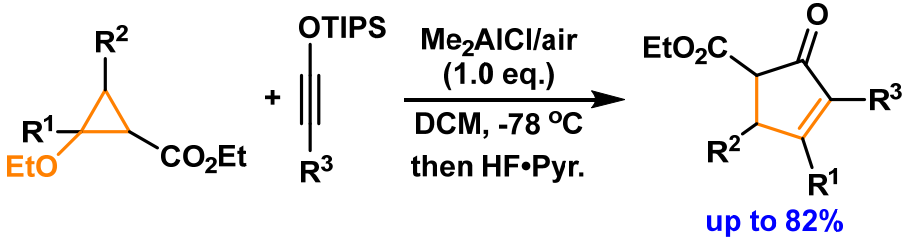
Org. Lett. **2014**, *16*, 5804.

➢ Cycloadditions & Formal Cycloadditions



Both EWG and EDG on the indole were tolerated

J. Am. Chem. Soc. **2007**, *129*, 9631.



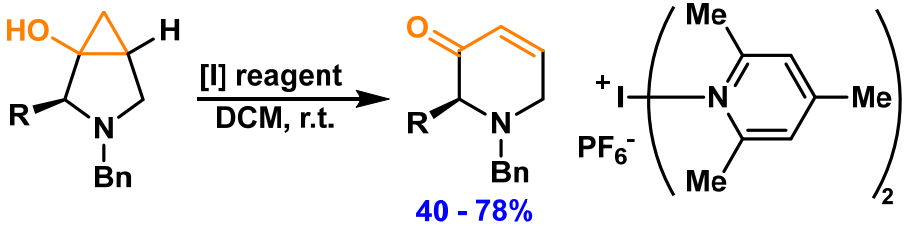
Older bottles of Me_2AlCl were more effective than the news

(MeO)AlMeCl

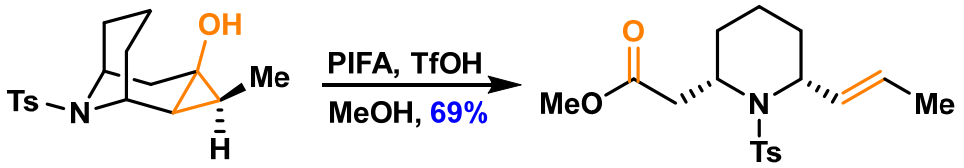
Angew. Chem. Int. Ed. **2008**, *47*, 7068.

Others

➢ Oxidative Ring Opening

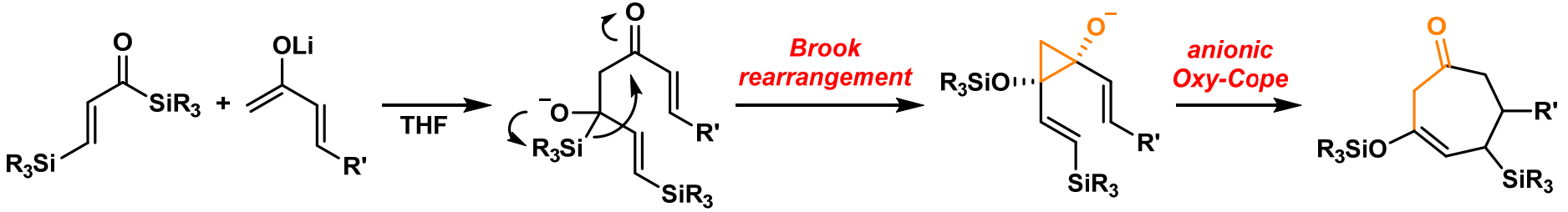


Eur. J. Org. Chem. **2008**, 4041.

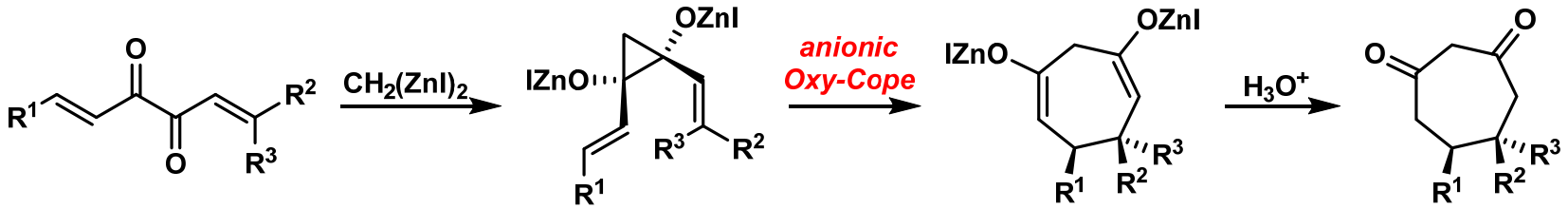


Yuki Gosei Kagaku Kyokaishi, **2004**, *62*, 919.

➢ Anion oxy-Cope Rearrangement

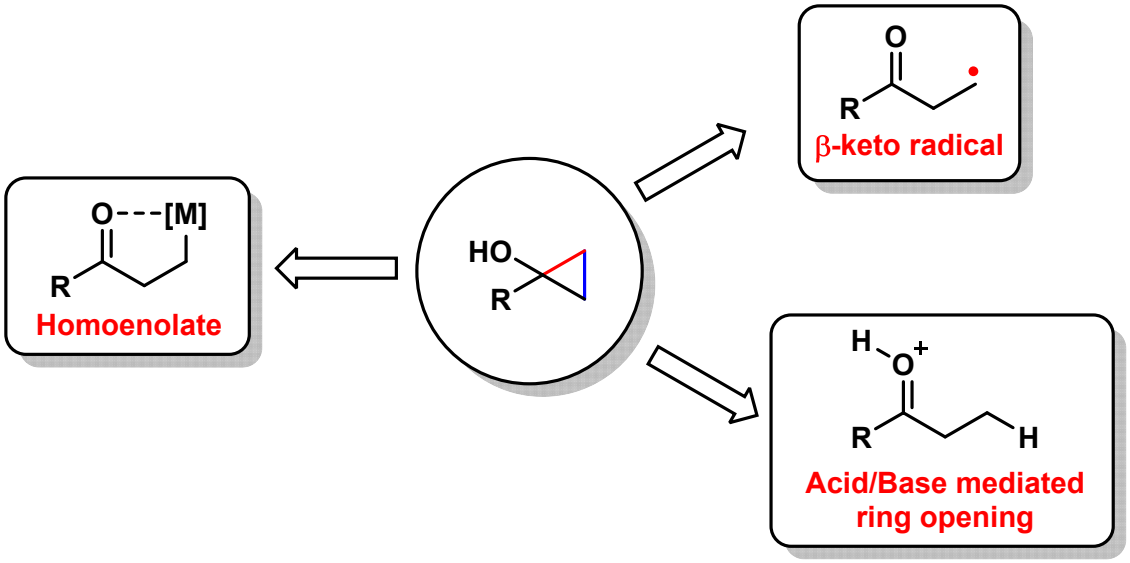


J. Am. Chem. Soc. **1995**, *117*, 6400.



Org. Lett. **2010**, *12*, 5204.

Summary


O
R
β-keto radical
O---[M]
R
Homoenolate
HO
R
H
O+
R
H
Acid/Base mediated
ring opening