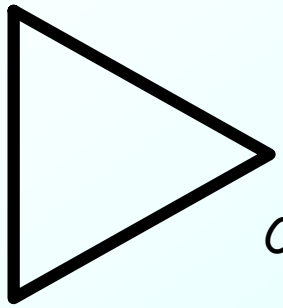
Enantioselective cyclopropanation methods

Mathieu CANDY

Bibliographic group-meeting

07.02.2008

Introduction



Cycle tension : +27.5 Kcal/mol

-Cyclopropanes have always fascinated organic chemists.

-They are present in more than 4000 natural products and in more than 100 commercial drugs.

- They are versatile synthetic intermediates.

Charette A. B. et *al. Chem. Rev.* **2003**, 977
Davies H. M. L. *Tetrahedron* **1993**, 5203
Nonhebel, D.C. *Chem. Soc. Rev.* **1993**. 347

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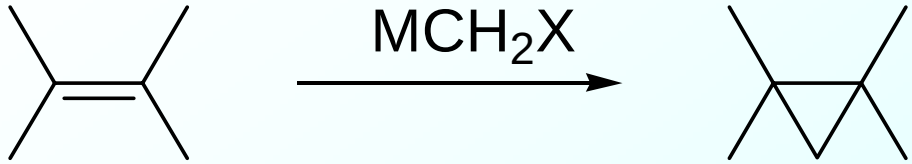
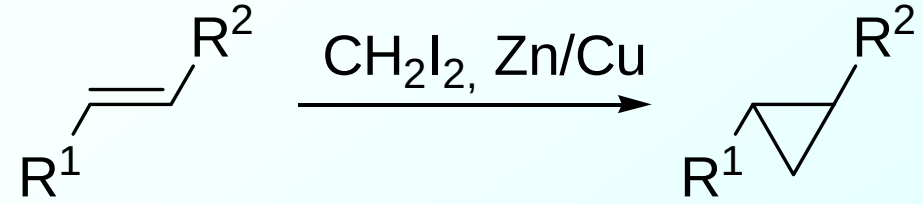
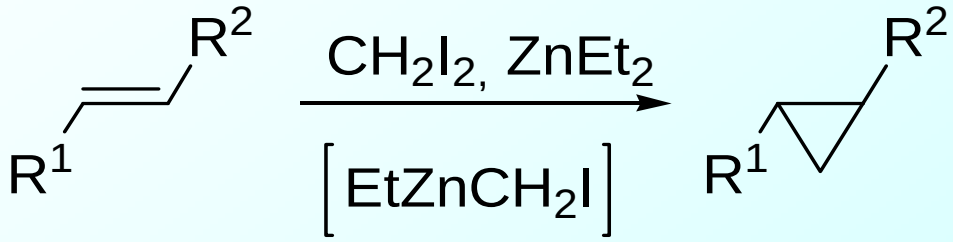
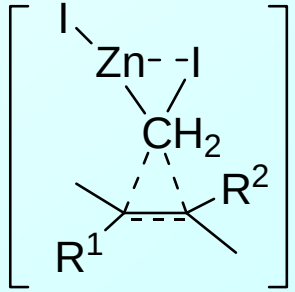
1. Halomethylmetal mediated cyclopropanation



-Simmons Smith Cyclopropanation





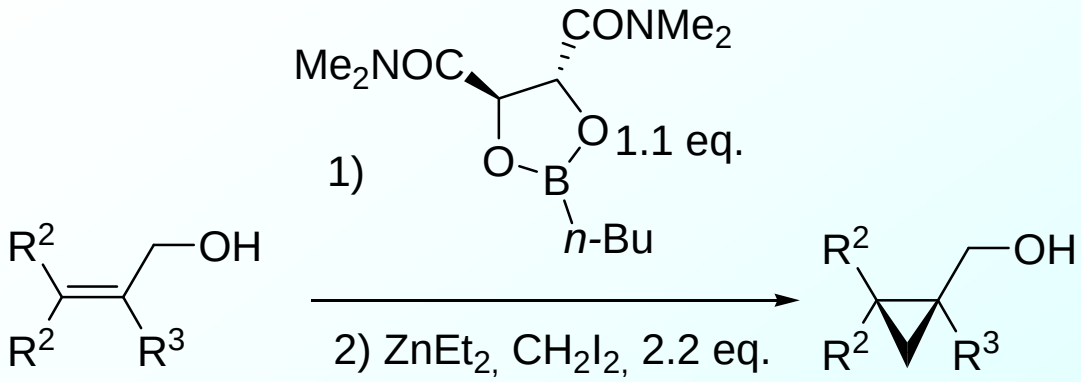


-Very good diastereoselectivity

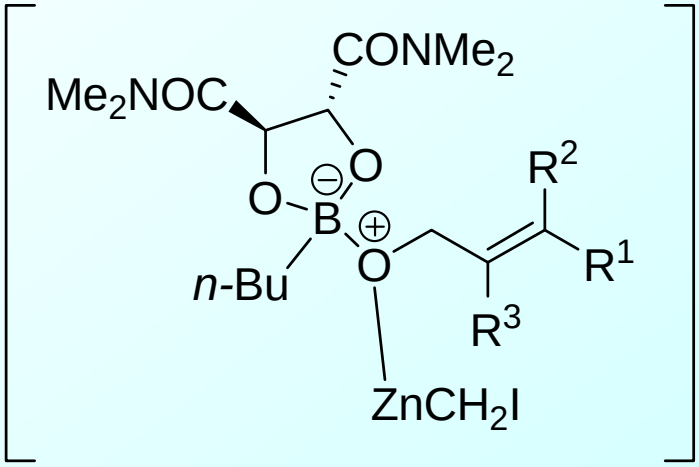
-Use of chiral auxiliaries

Simmons, H.E. et *al. J. Am. Chem. Soc.* **1958**, 5323
Furukawa, J. et *al. Tetrahedron Lett.* **1966**, 3353.

1. Halomethylmetal mediated cyclopropanation



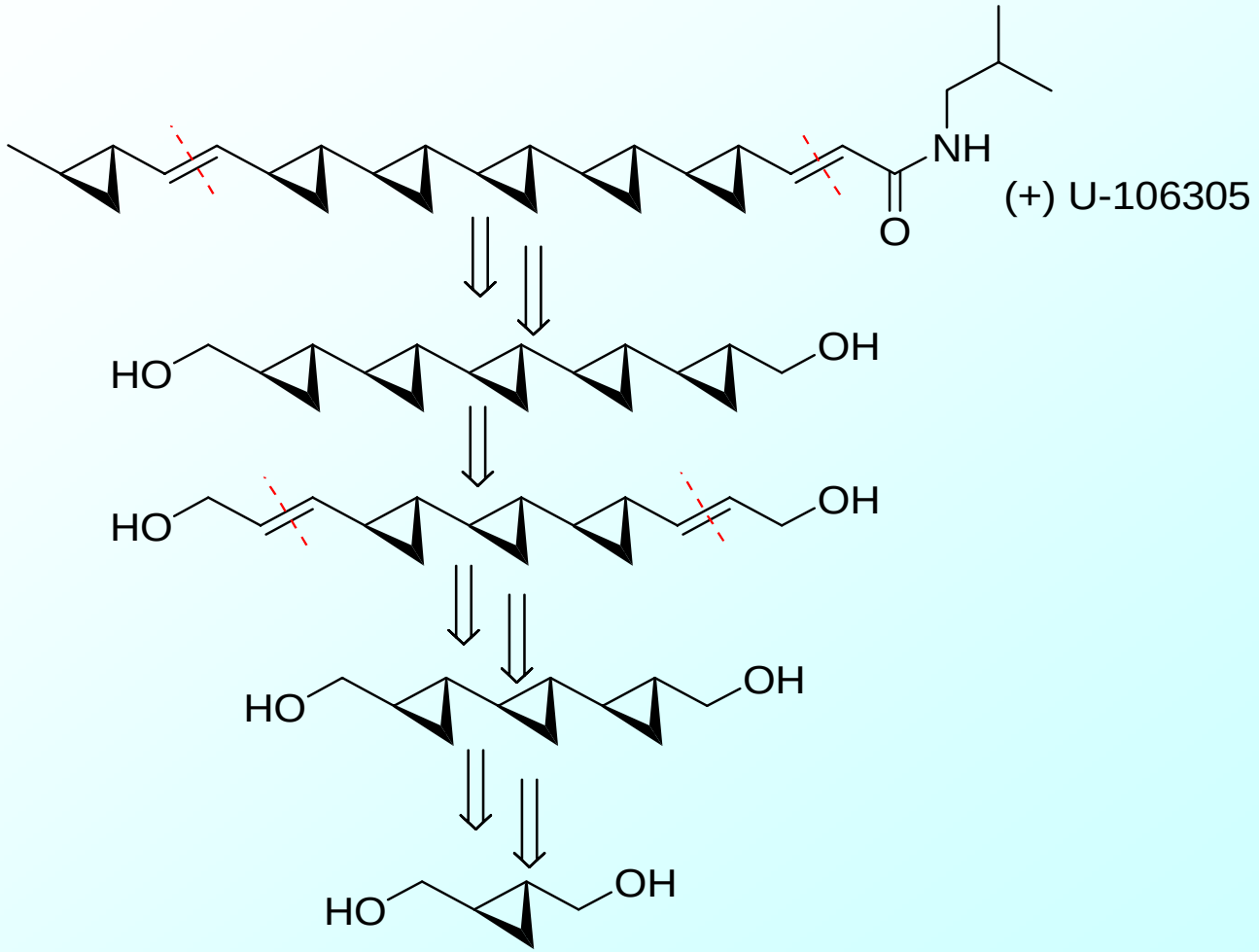
Yield : 73-98 % / ee : 85-94 %



Charette A.B. et *al* . *J. Am. Chem. Soc.* **1994**, 2651.

1. Halomethylmetal mediated cyclopropanation

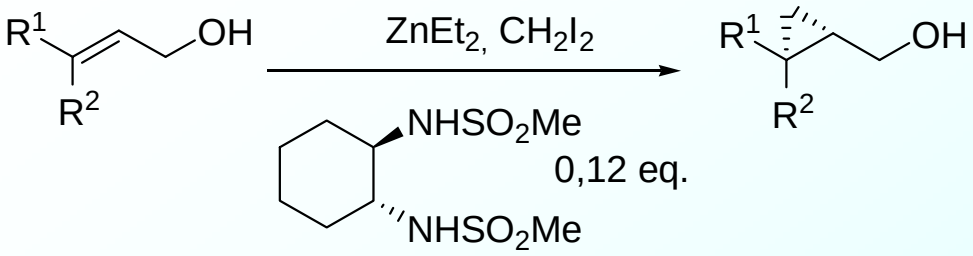
Application to the total synthesis of (+) U-106305 :



Charette A.B. et *al* . *J. Am. Chem. Soc.* **1996**, 10327.

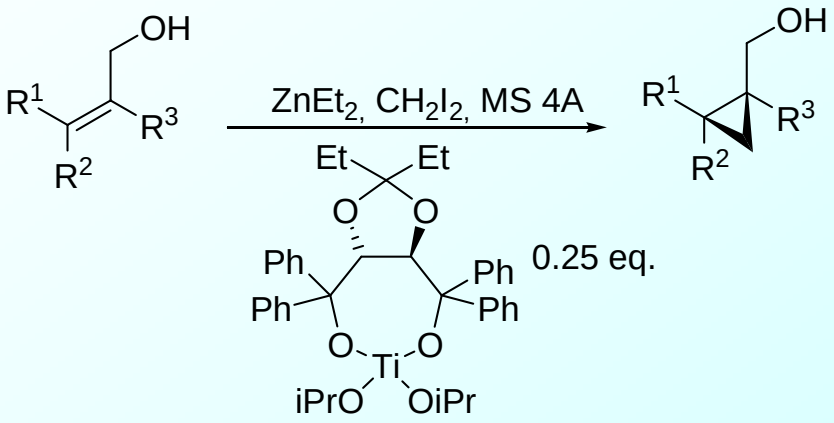
1. Halomethylmetal mediated cyclopropanation

- Chiral catalysts



Yield : 81-93 %, ee : 72-89 %

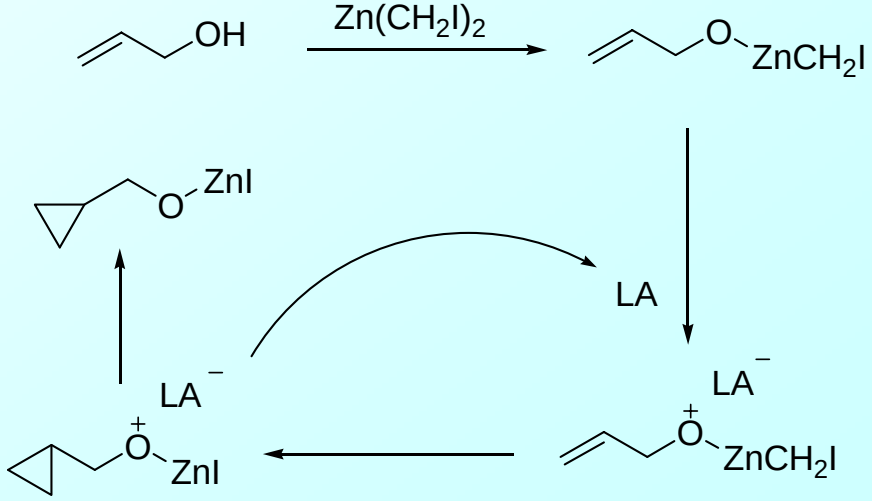
Denmark, J. et *al. Tetrahedron lett.* **1992**, 2575



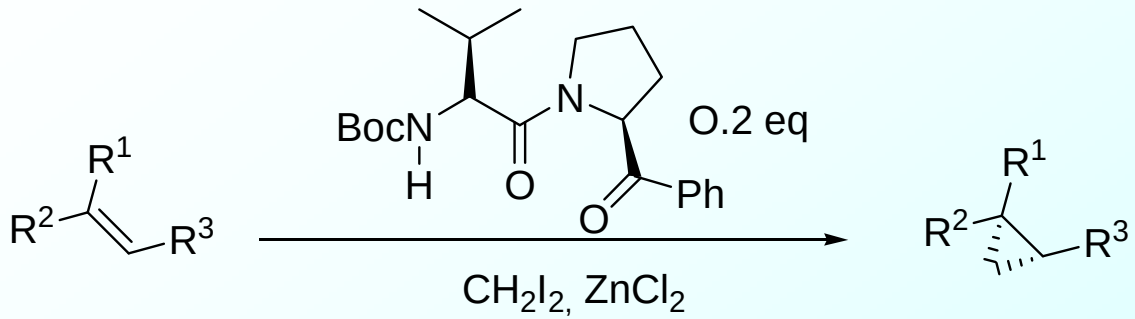
Yield : 60-90 %, ee : 50-92%

Charette, A. B. et *al. J. Am. Chem. Soc.* **2001**, 12168

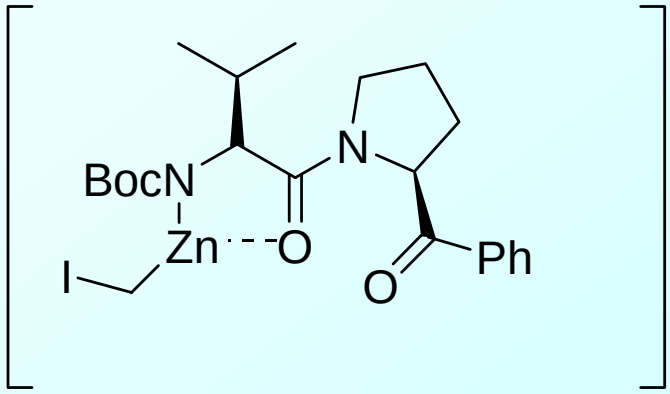
Catalytic cycle :



1. Halomethylmetal mediated cyclopropanation

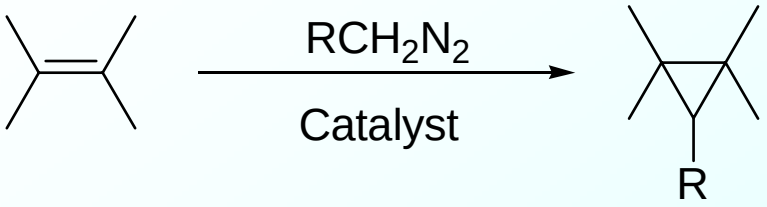


Yield : 43-84 % ee : 72-91 %



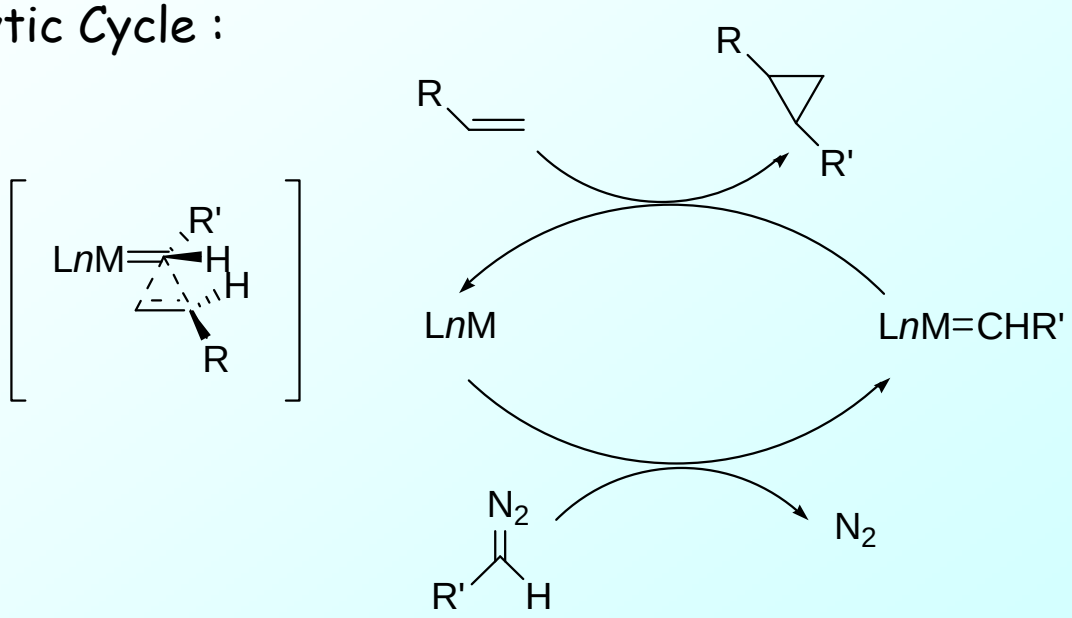
Shi, Y. et *al. Org. Lett.* **2006**, 2827

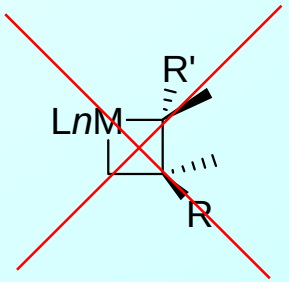
2. Transition metal catalyzed decomposition of diazoalkanes



-Transition metal used : Cu, Ru, Rh, Co for electron-rich olefins and Pd for electron-poor olefins.

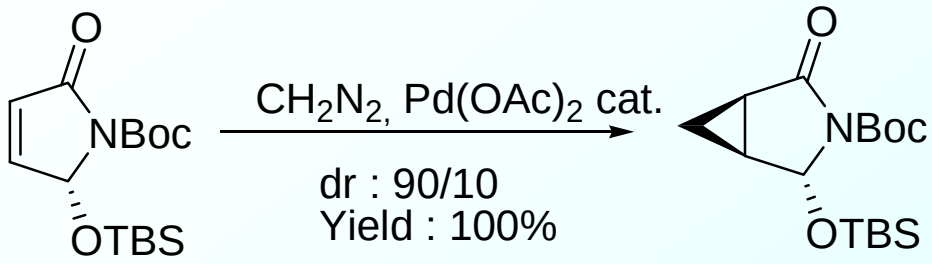
Catalytic Cycle :



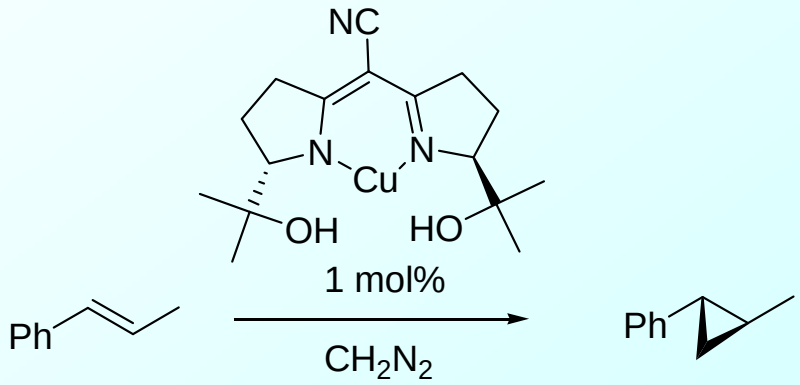


Charette A. B. et *al. Chem. Rev.* **2003**, 977

2.1. Decomposition of diazomethane



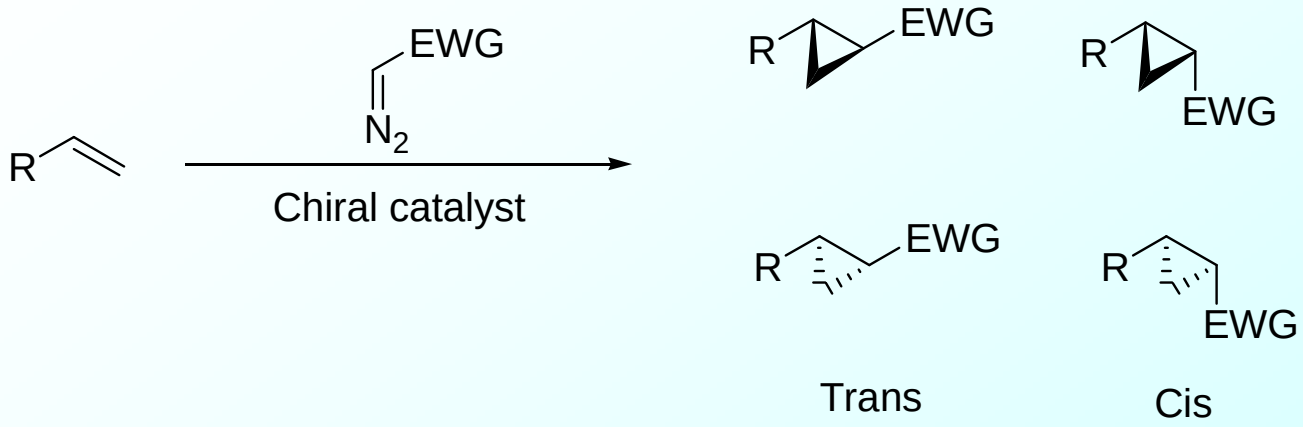
Ohfune, Y. et *al. J. Org. Chem.* **1991**, 4167



Yield : 75% ee : 45%

Jacobsen, E. et *al. Springer-Verlag : Berlin,* **1999**, Vol II, P513

2.2. Diazoalkanes bearing one electron-withdrawing group



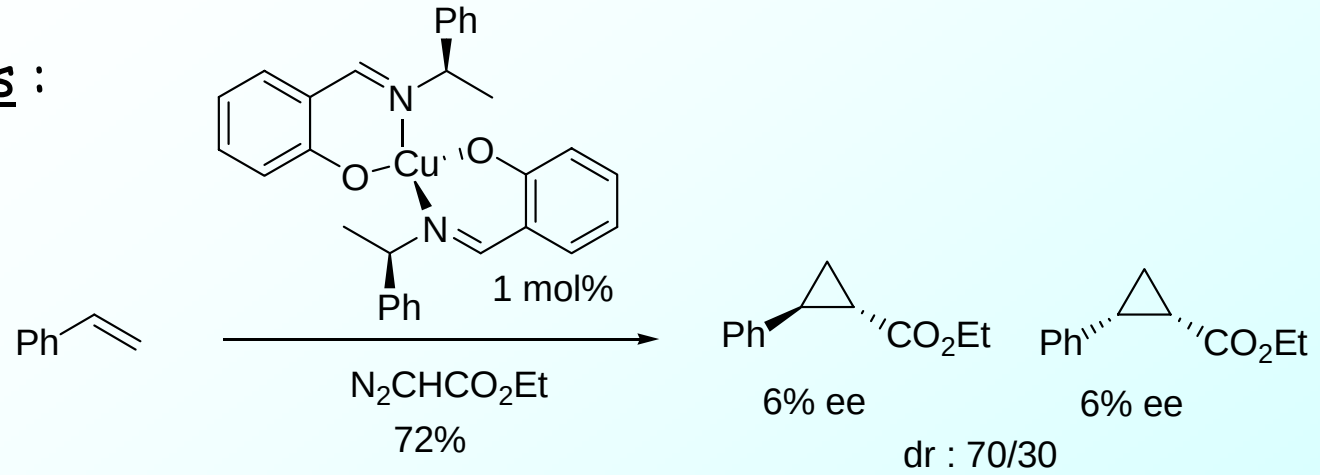
- Incredibly large number of chiral complexes tested

- No universal catalyst : ee and dr depend on both the nature of the diazoalkane and the starting olefin

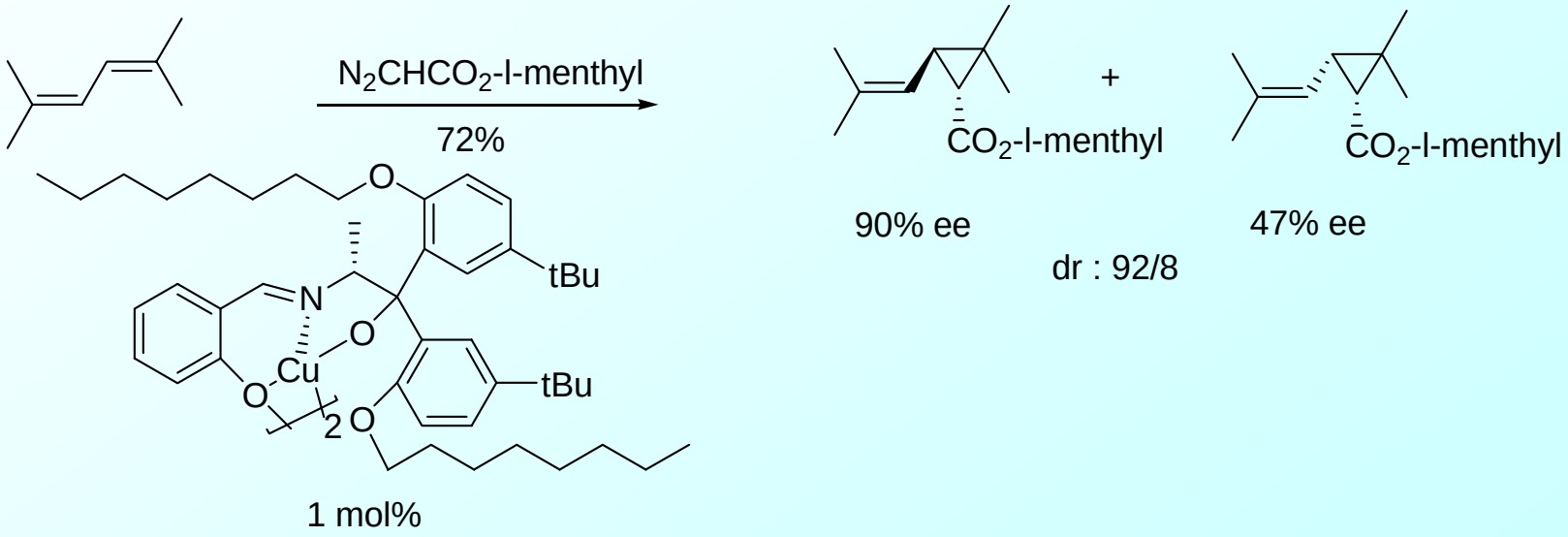
- General conclusions : - Cu, Rh and Ru are the best catalysts for the preparation of *trans* isomers.
  - Co catalysts are the best to obtain *cis* isomers
  - Cu and Rh are the most active catalysts

2.2. Diazoalkanes bearing one electron-withdrawing group

<u>Cu Catalysts</u> :



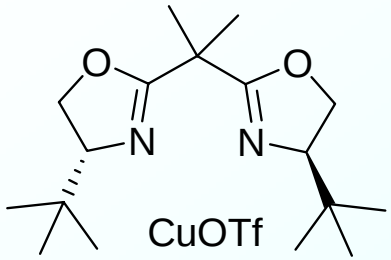
Nozaki, H. et *al. Tetrahedron Lett.* **1966**, 5239



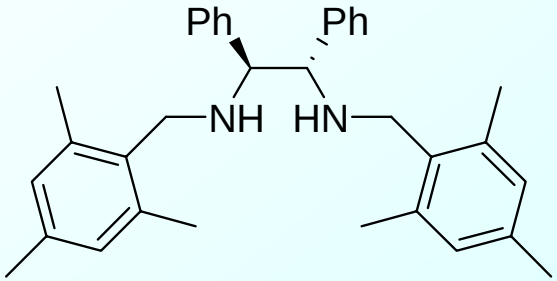
Aratani, T. et *al. Tetrahedron Lett.* **1977**, 2599

2.2. Diazoalkanes bearing one electron-withdrawing group

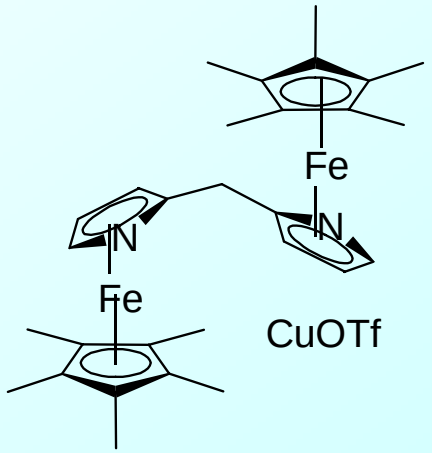
Some of the best copper chiral ligands for the cyclopropanation of styrene



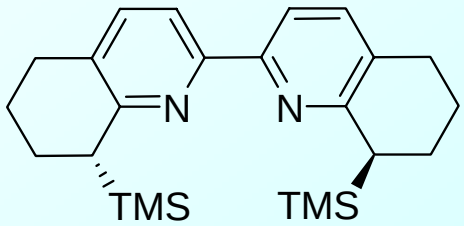
dr : 94/6, 99% ee (trans)
Evans, 1991



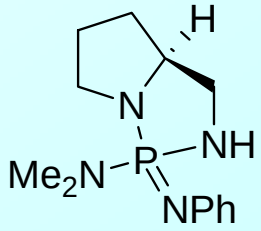
$Cu(OTf)_2$, $PhNHNH_2$
dr : 97/3, 96% ee (trans)
Kanemasa, 1994



dr : 96/4, 94% ee (trans)
Fu, 1998



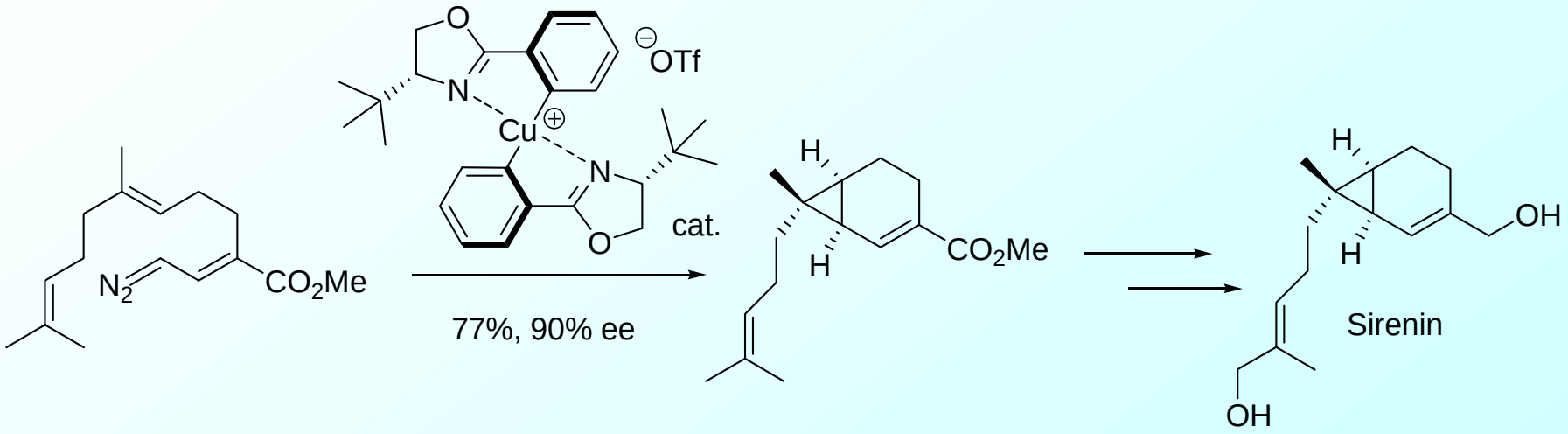
CuOTf
dr : 86/14, 92% ee (trans)
Katsuki, 1993



CuOTf
dr : 99/1, 94% ee (trans)
Buono, 1999

2.2. Diazoalkanes bearing one electron-withdrawing group

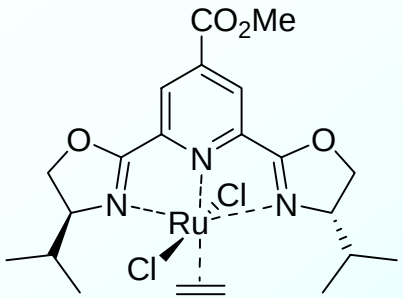
Example of intramolecular cyclopropanation :



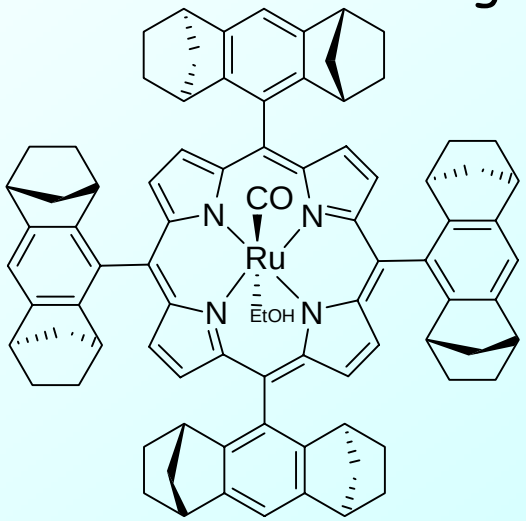
Corey, E. J. et *al. Tetrahedron Lett.* **1995**, 8745

2.2. Diazoalkanes bearing one electron-withdrawing group

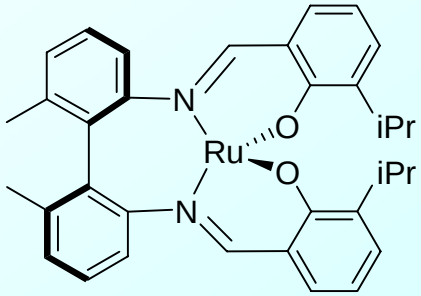
Ru catalysts : - Less reactive than Cu or Rh ones
- Pybox is the more feasible and studied ligand



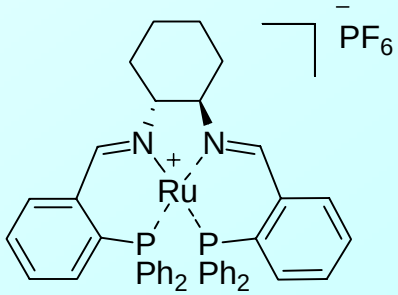
dr : 94/6, 97% ee (trans)
Nishiyama, 1995



dr : 97/3, 98% ee (trans)
Che 1997



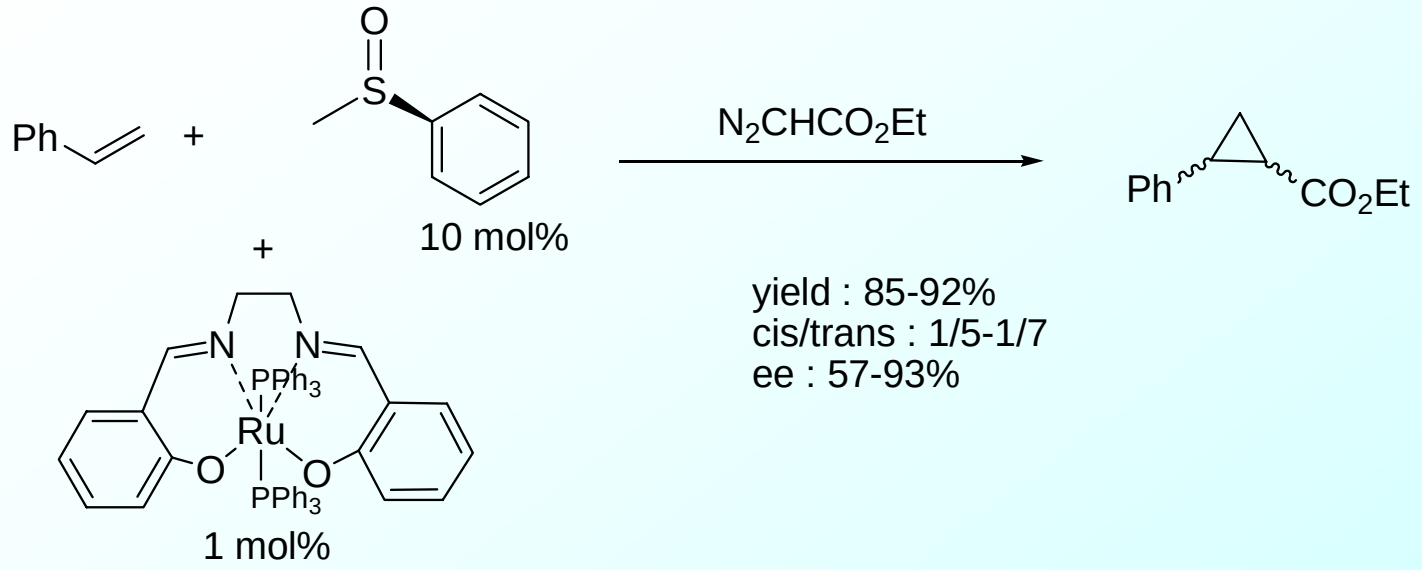
dr : 98/2, 95% ee (trans)
Scott 2001



dr : 17/83, >99% ee (cis)
Mezetti 2001

2.2. Diazoalkanes bearing one electron-withdrawing group

Ru catalysts :



yield : 85-92%
cis/trans : 1/5-1/7
ee : 57-93%

-The Lewis base as ligand activates the reactivity of the Ru carbene

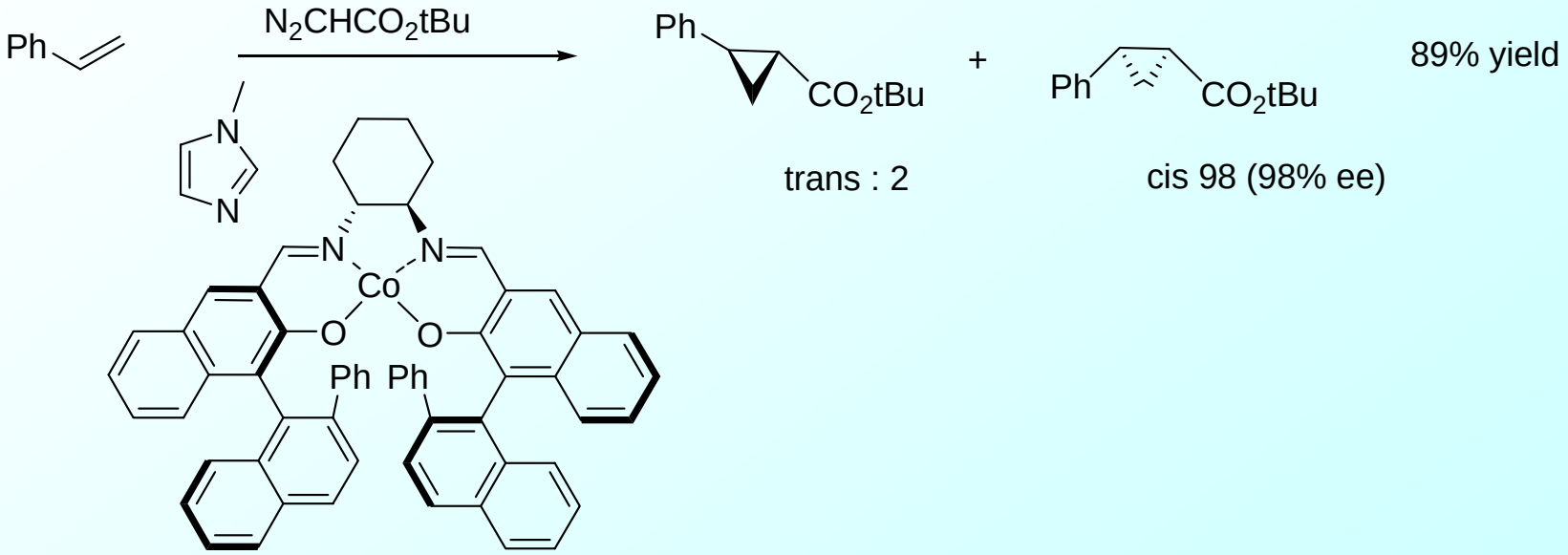
- Possible screening of Ru complexes

Nguyen, S. T. et *al. Angew. Chem. Int. Ed.* **2005**, 3885

2.2. Diazoalkanes bearing one electron-withdrawing group

Co catalysts :

- Less reactive and less used than other transition metals
- Good results in *cis* diastereoselectivity



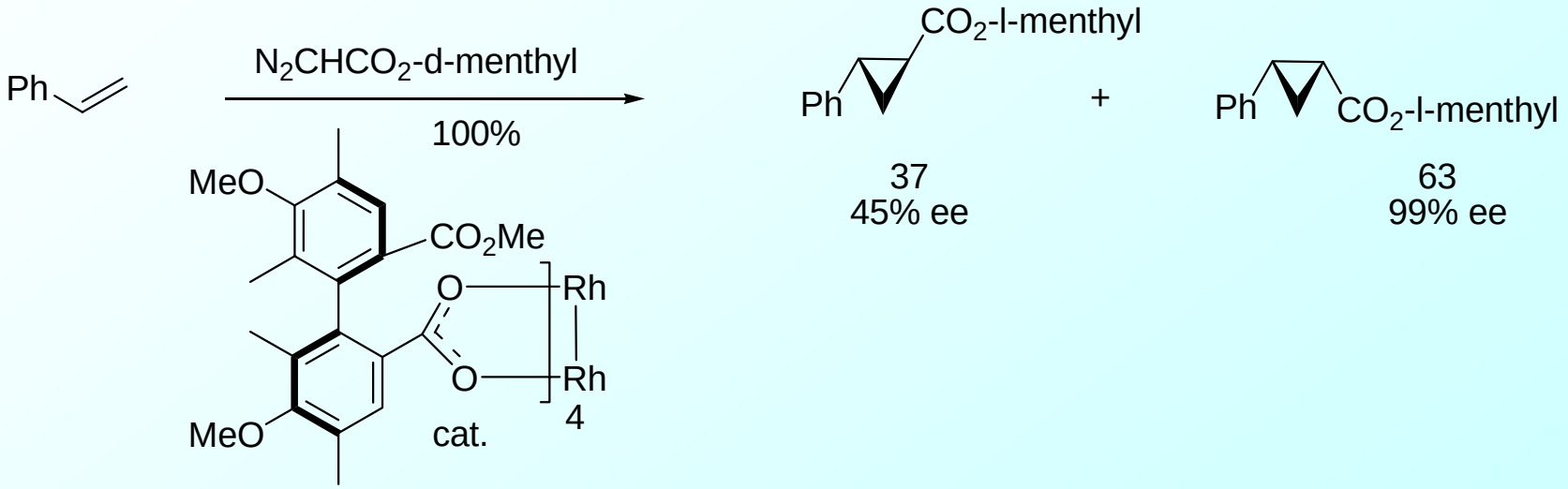
Katsuki, T. et *al. Tetrahedron* **1997**, 5936.

2.2. Diazoalkanes bearing one electron-withdrawing group

Rh catalysts :

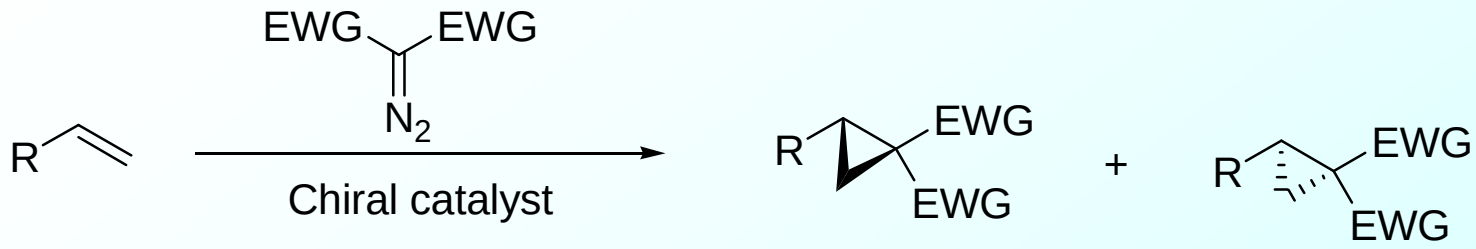
- Very efficient catalyst but less diastereoselective than other metals

- Generaly dirhodium complexes with carboxylates or carboxamidates

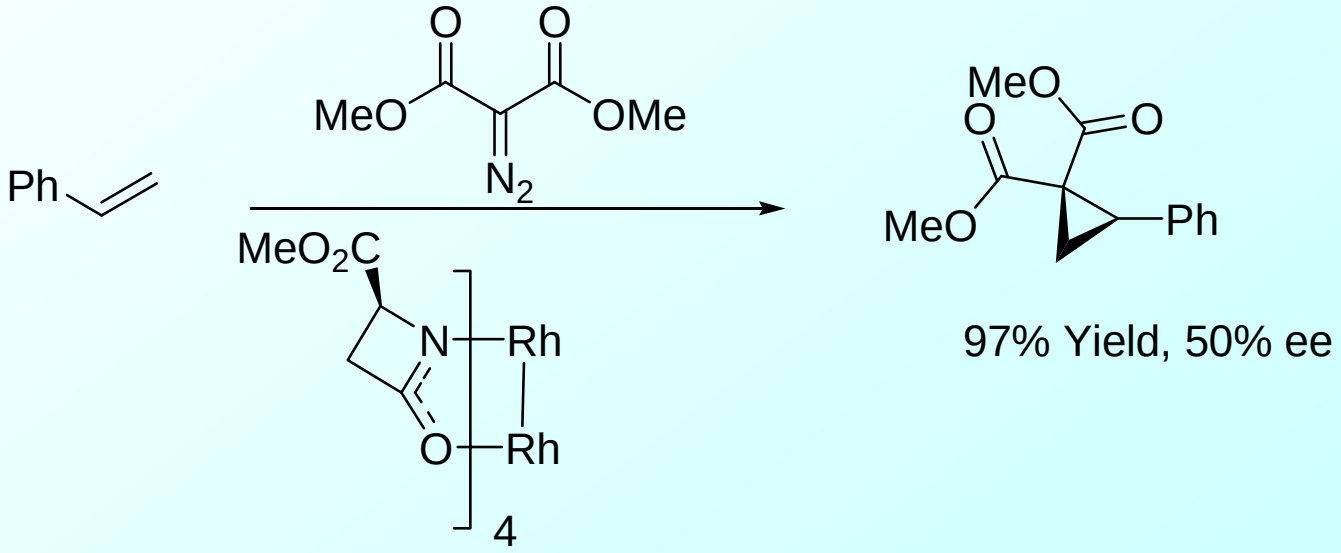


Achiwa, K. et *al. Synlett* **1997**, 781

2.3. Diazoalkanes bearing two electron-withdrawing groups



- Significally less reactive than diazoalkanes with one EWG
- More active catalysts are required (such as Rh or Cu)

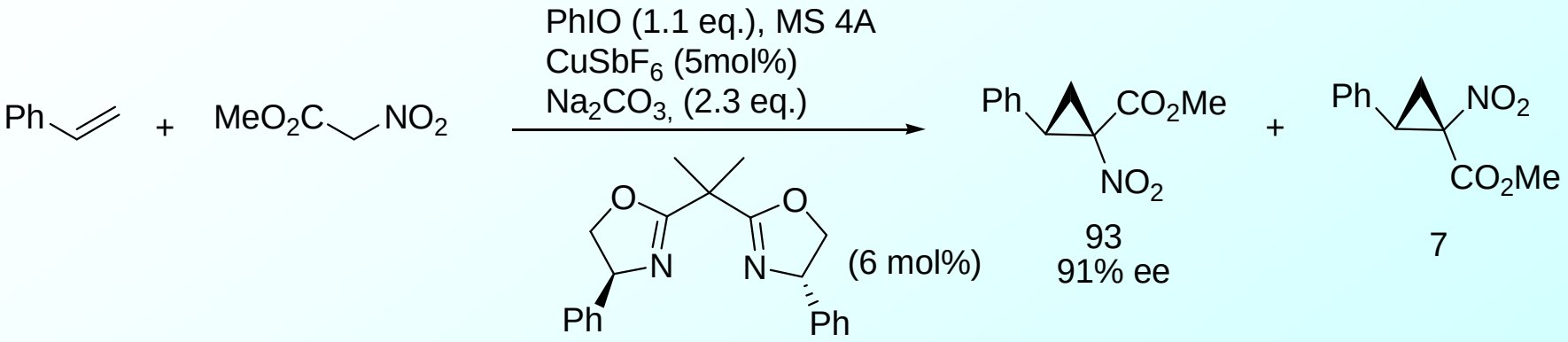


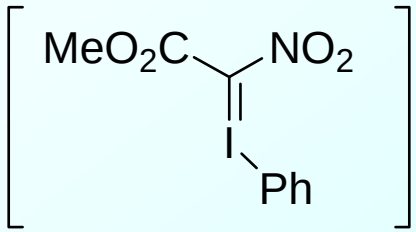
97% Yield, 50% ee

Doyle, M. P. et *al. Org. Lett.* **2000**, 1145

2.3. Diazoalkanes bearing two electron-withdrawing groups

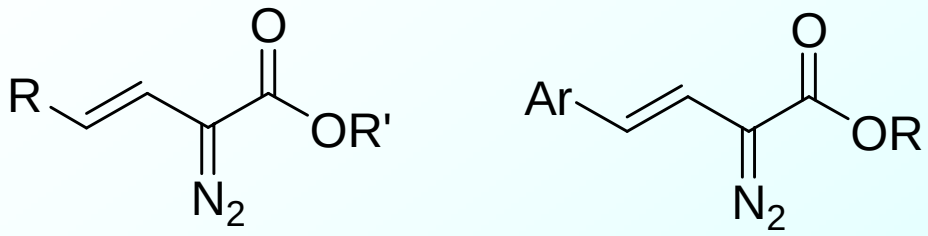
Alternative : *In situ* formation of an iodonium Ylide, precursor of the metal carbene





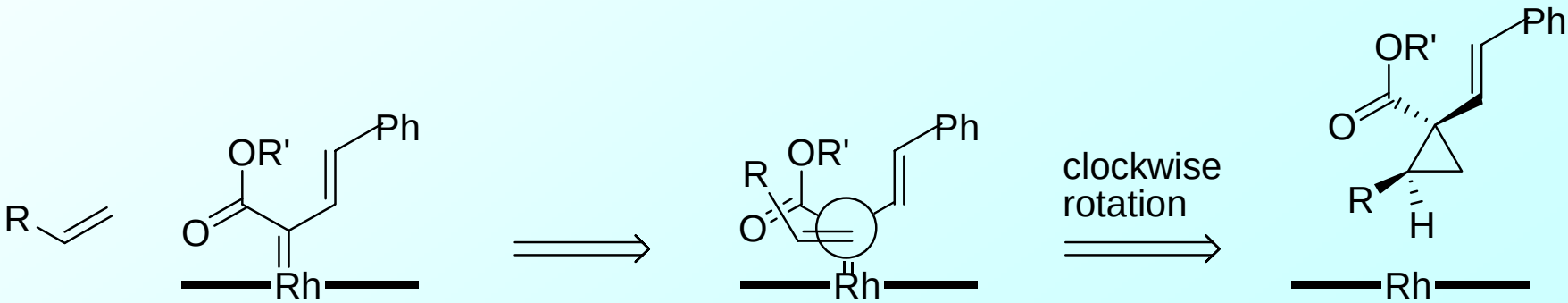
Charette, A. B. et *al. J. Am. Chem. Soc.* **2005**, 18014

2.3. Aryl- and vinyldiazoesters

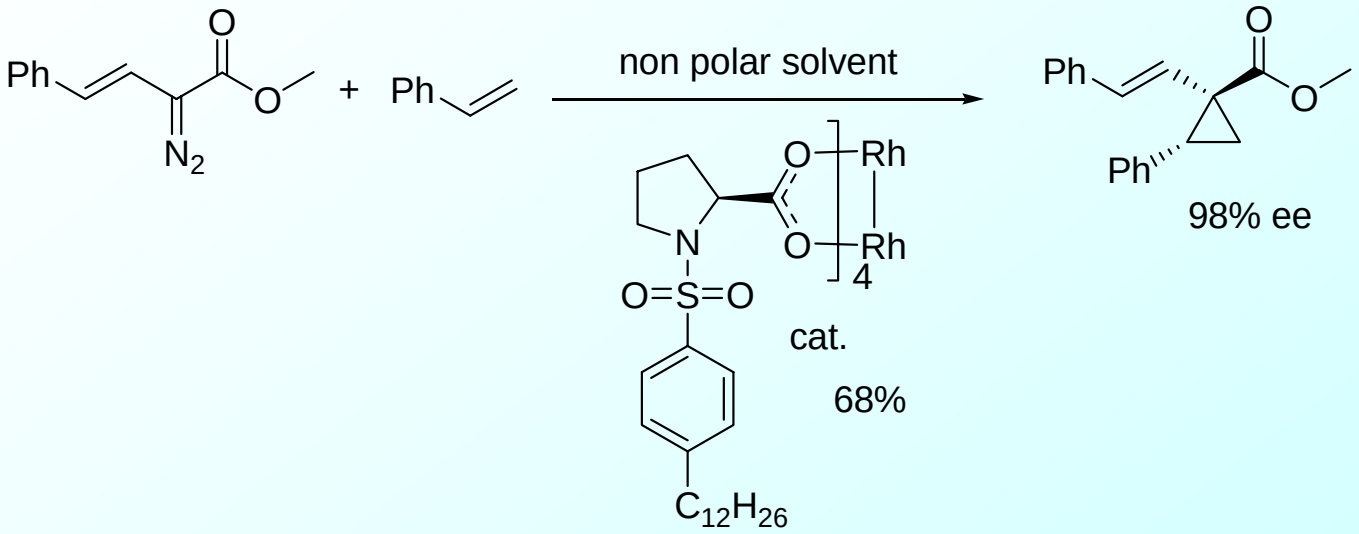


- Moderate reactivity
- Rh complexes are the best catalysts with high level of diastereocontrol
- Use of non polar solvents
- Do not react with *E* disubstitued olefins

- Origin of the diastereoselectivity :

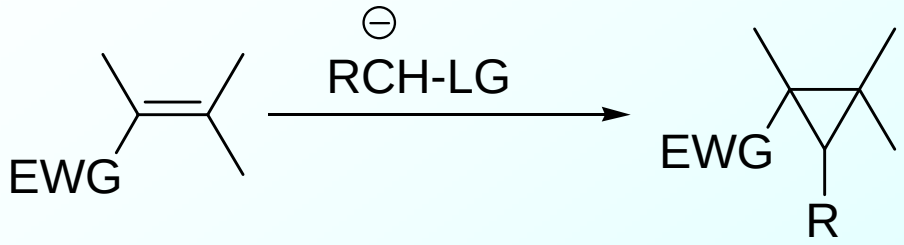


2.3. Aryl- and vinyldiazoesters

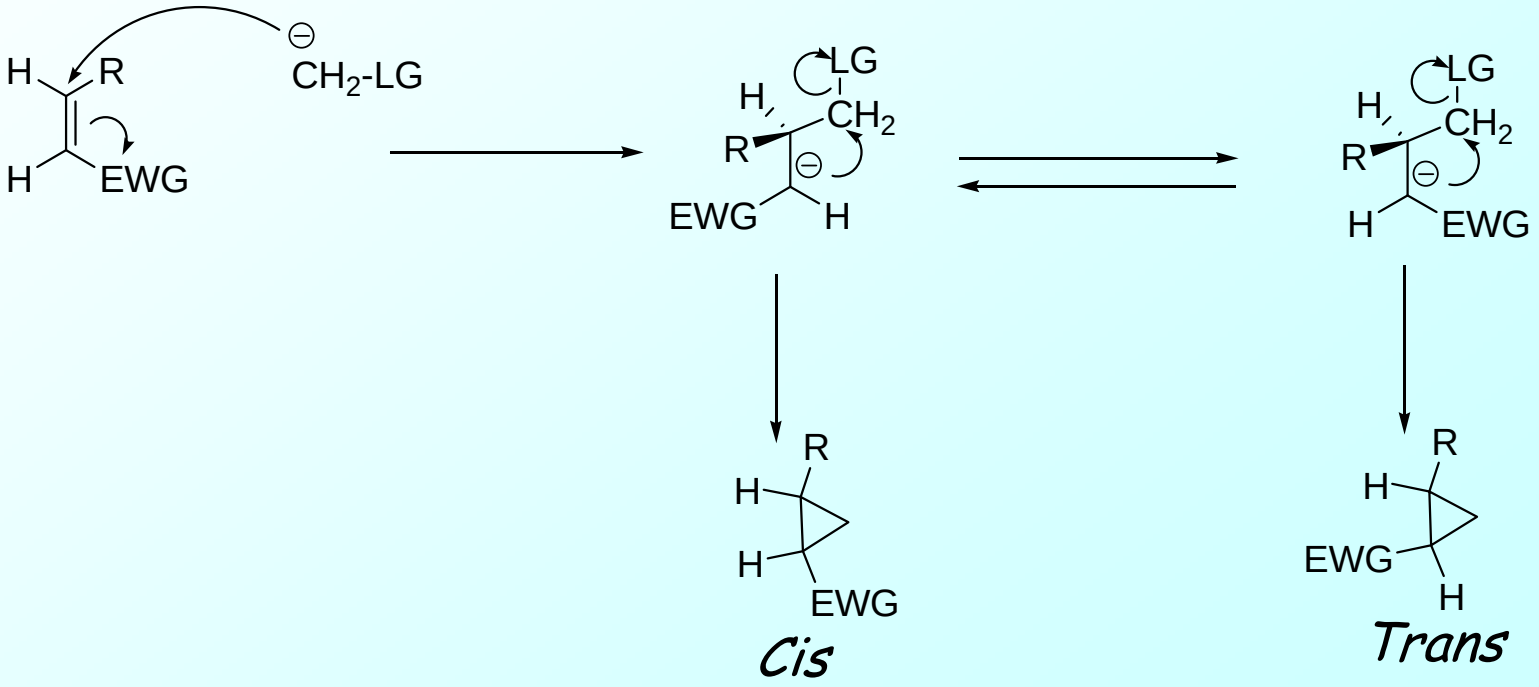


Davies, H. M. L. et *al. J. Am. Chem. Soc.* **1993**, 9468

3. Michael initiated ring closure (MIRC)



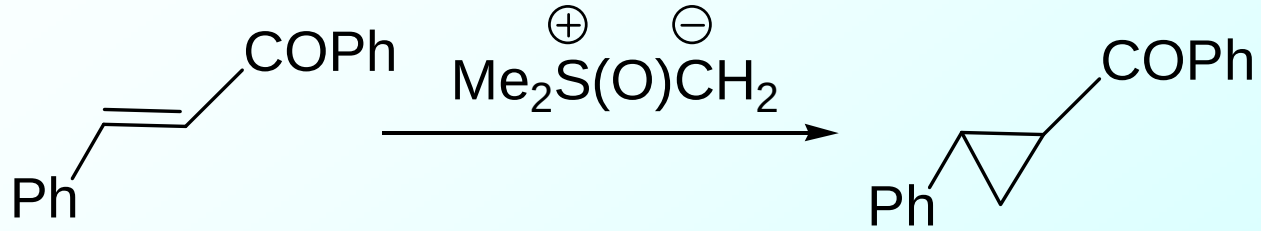
- Both *E* and *Z* olefins give *trans* cyclopropanes in general



3.1 Sulfur ylides

- First reported by Hartmann in 1950

- Used by Corey and Chaykovsky in 1962



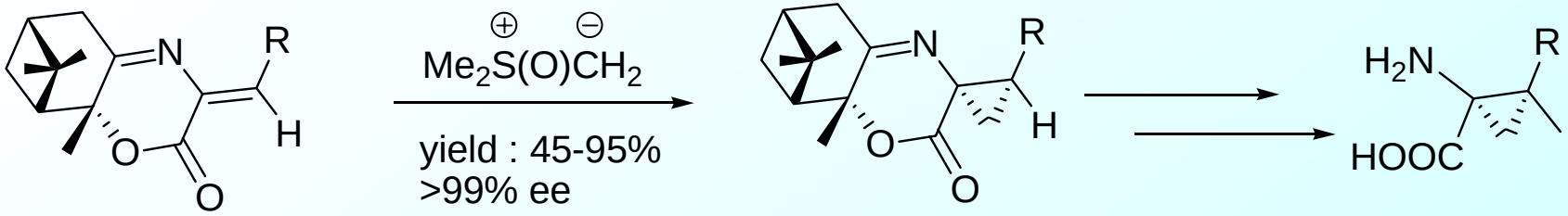
- Me_2SCH_2 reacts with ketones and aldehydes to give oxirans !!!

Corey, E. J. ; Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, 867

3.1 Sulfur ylides

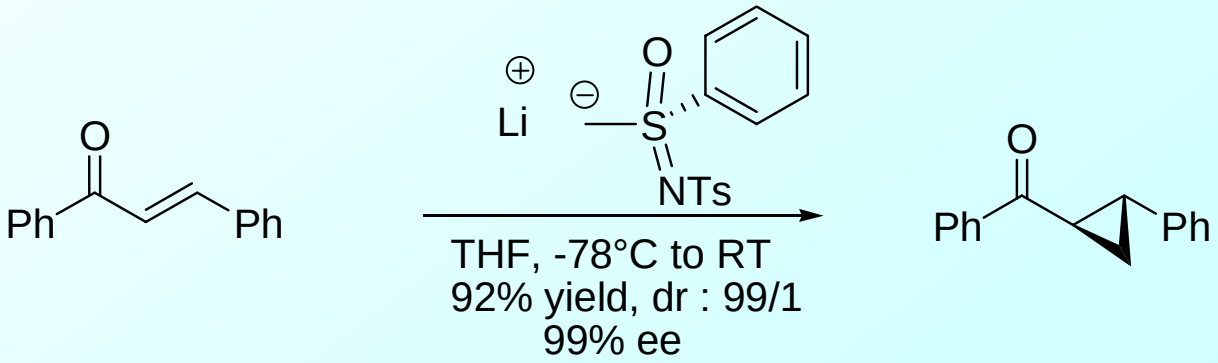
- General very good diastereoselectivity with cyclic Michael acceptors

- Use of chiral auxiliaries



Calmes, M. et *al. Tetrahedron asymmetry,* **1997**, 395.

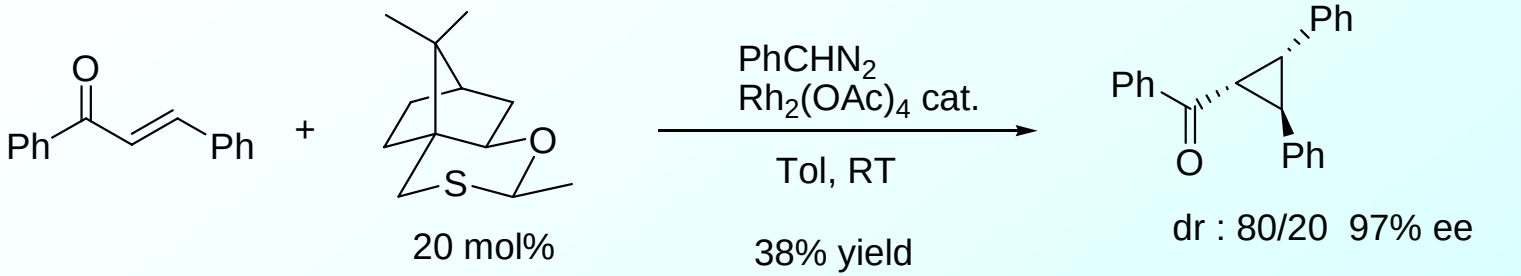
- Use of chiral sulfur ylides

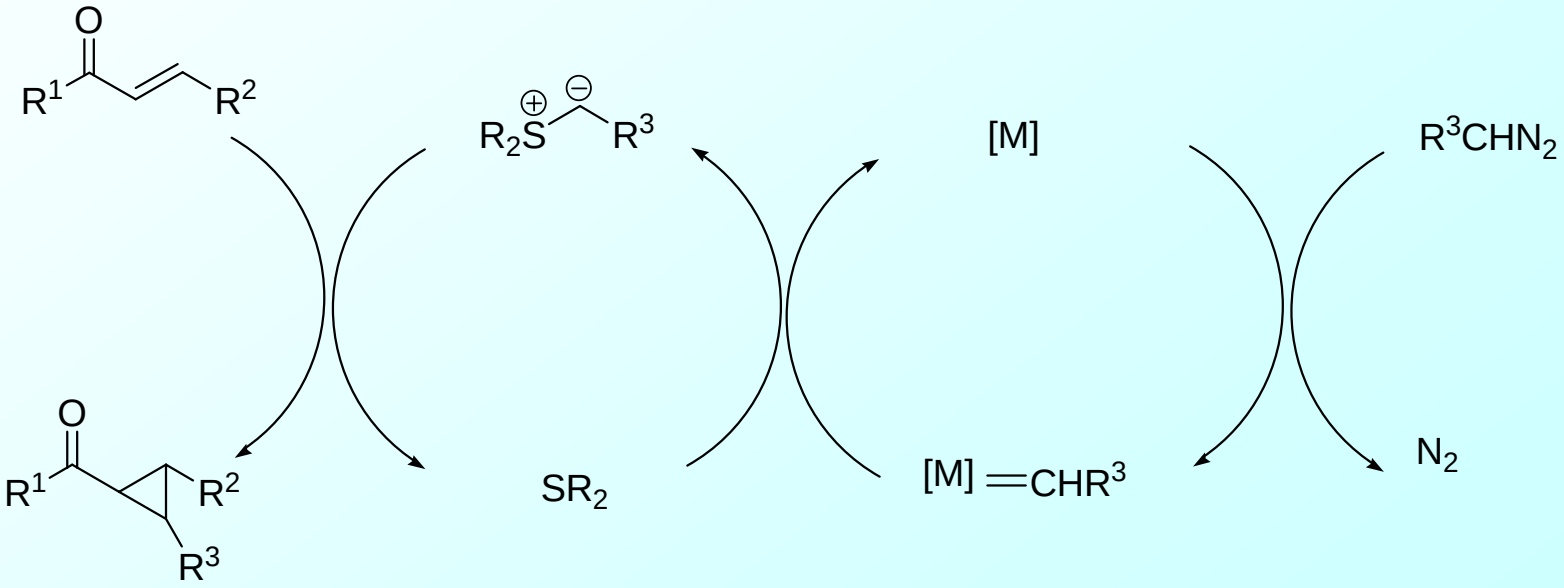


Pyne, S. G. et *al. J. Org. Chem.* **1997**, 2337

3.1 Sulfur ylides

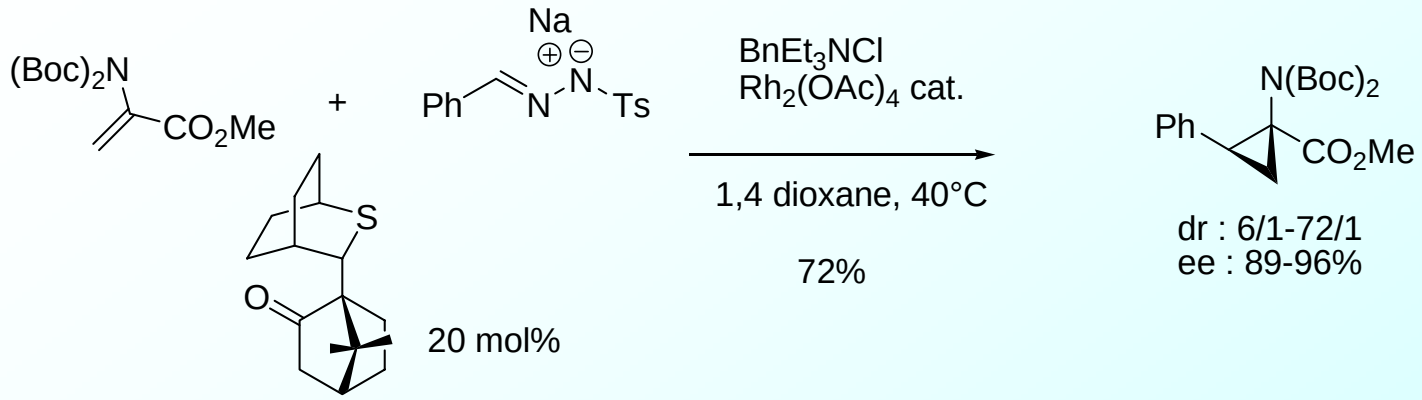
- Catalytic amount of chiral sulfid



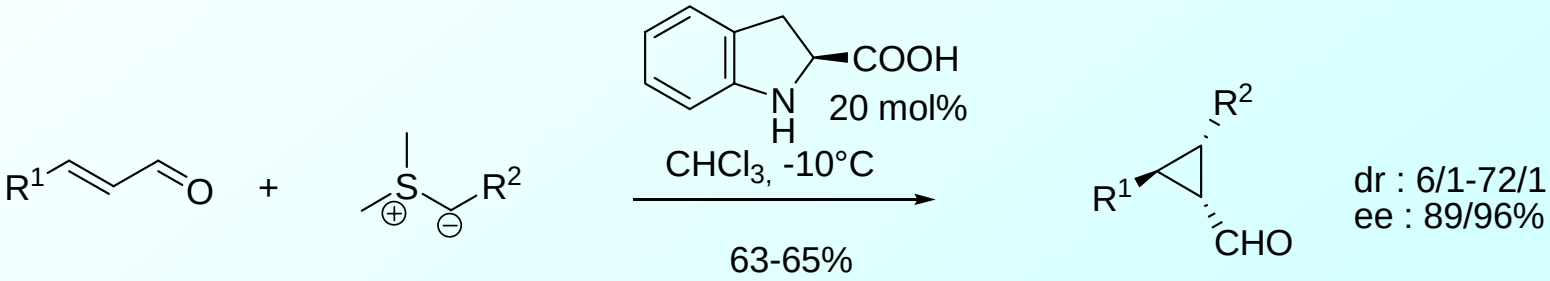


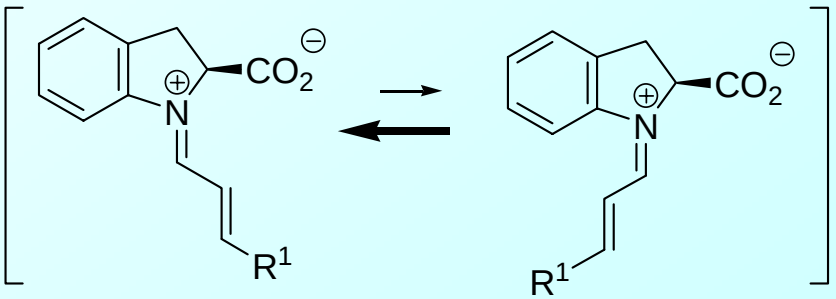
Aggarwal, V. K. et *al. Phosphorus, Sulfur, Silicon, Relat. Elem.* **1994**, *283*

3.1 Sulfur ylides



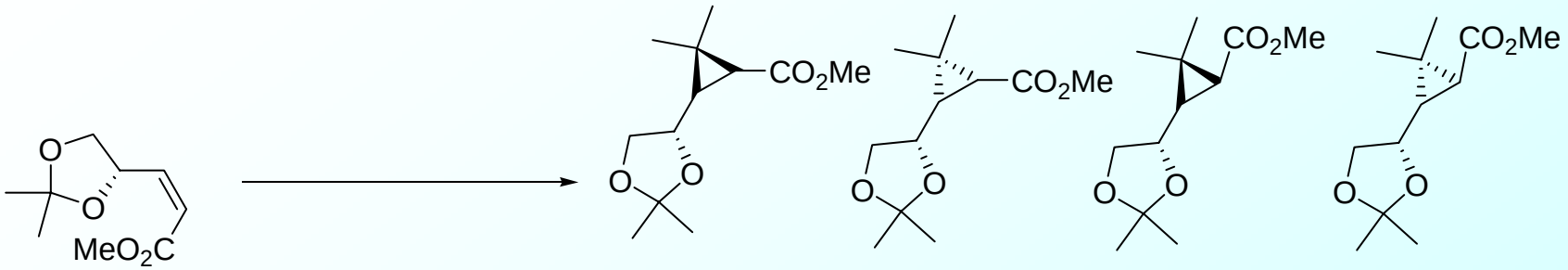
Aggarwal, V. K. et *al. Angew. Chem. Int. Ed.* **2001**, 1433





MacMillan, W. C. et *al. J. Am. Chem. Soc.* **2005**, 3240

3.2 Phosphorus ylides



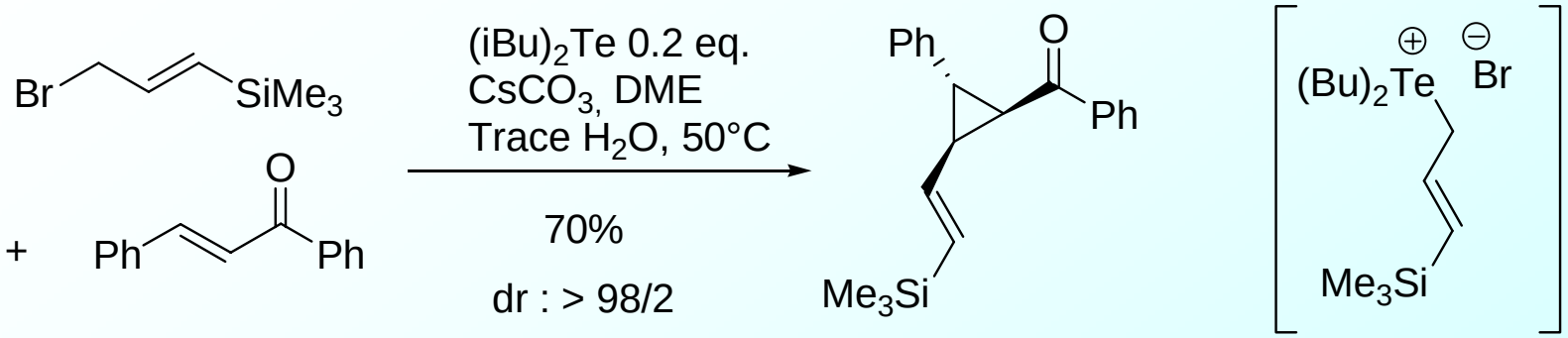
$Ph_3P{=}CMe_2$ (61%)	0	0	6	94
$Ph_2S{=}CMe_2$ (84%)	2	98	0	0

- Formation of anti cyclopropanes from *Z* olefins

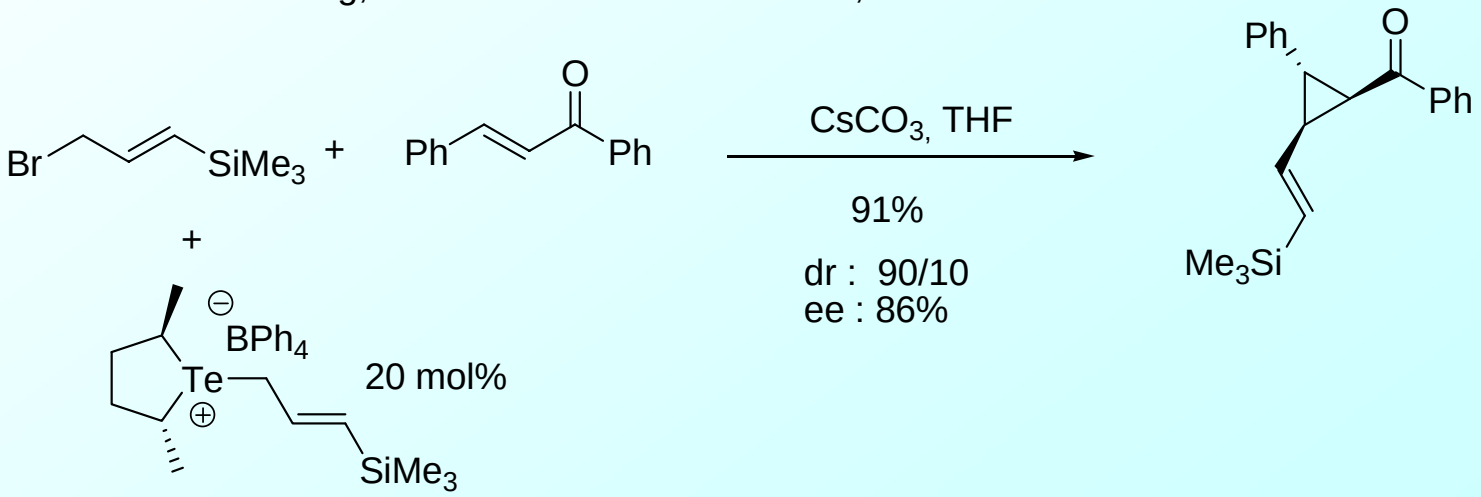
- No enantioselective reaction reported

Krief, A. et *al. Tetrahedron,* **1989**, 3039

3.3 Telluronium ylides

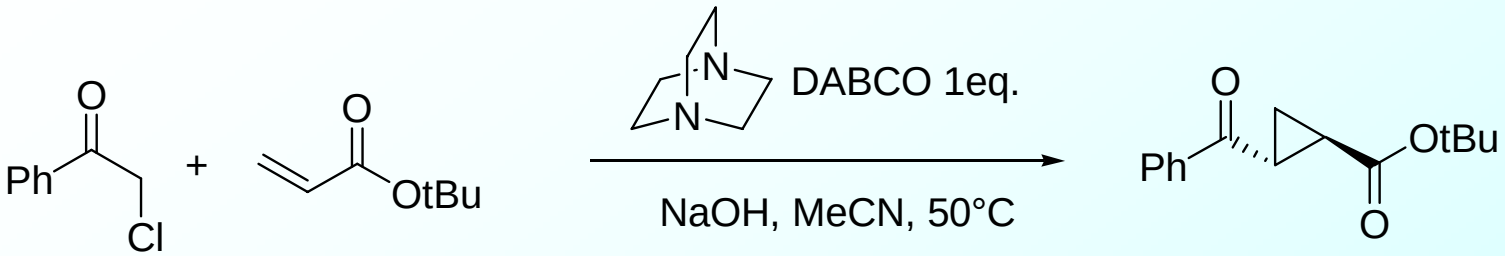


Huang, Y. Z. et al. *J. Chem. Soc. Chem. Commun.* **1993**, 7
For a review see : Huang, Y. Z. et *al. Tetrahedron* **1998**, 5667

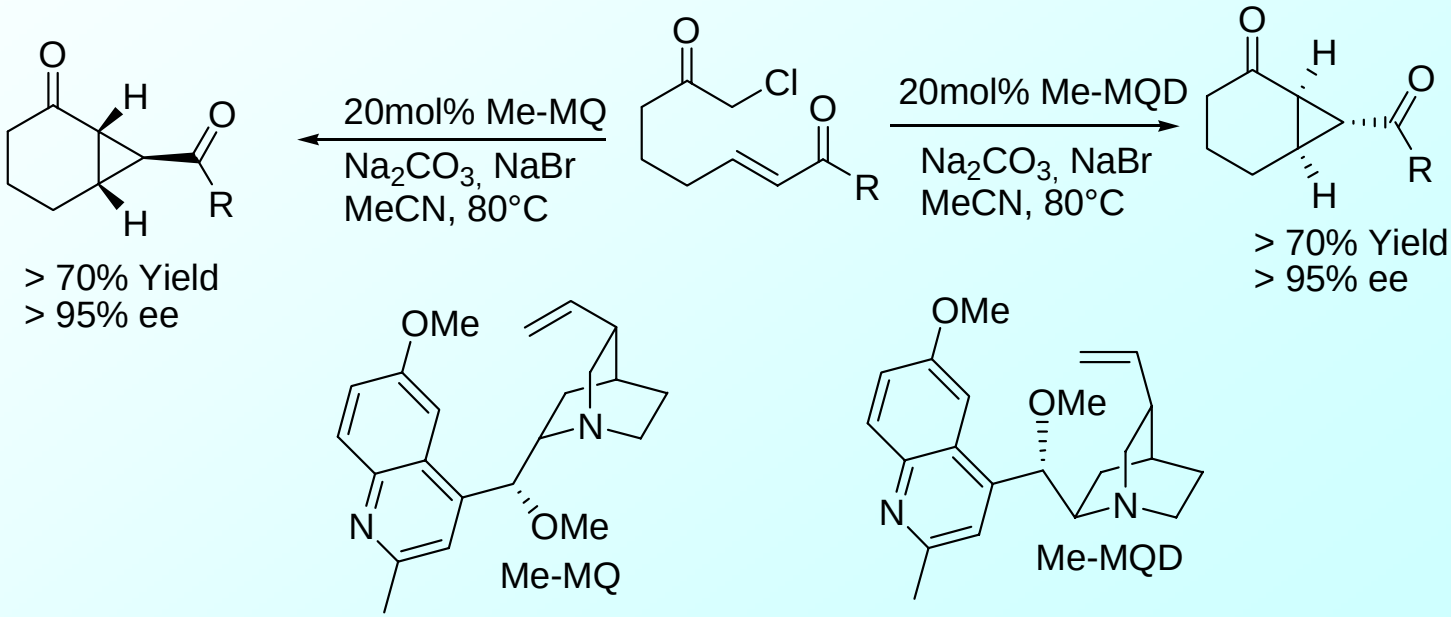


Yong, T. et *al. J. Am. Chem. Soc.* **2003**, 13030

3.4 Nitrogen ylides



Gaunt, M. J. et *al. Angew. Chem. Int. Ed.* **2003**, 828



Gaunt, M. J. et *al. Angew. Chem. Int. Ed.* **2006**, 6024