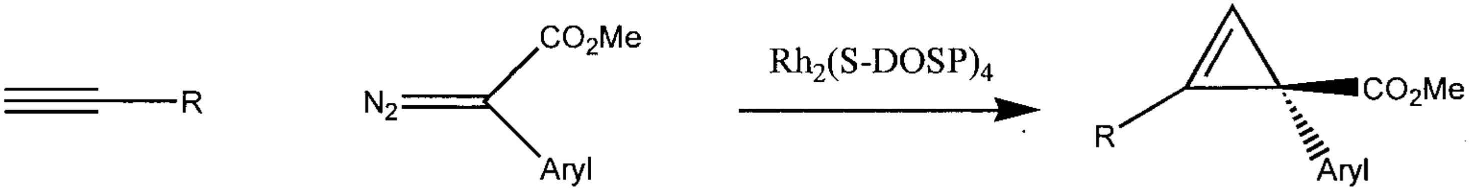
Dirhodium(II)Tetra (N-(dodecylbenzenesulfonyl)prolinate) Catalyzed Enantioselective Cyclopropenation of Alkynes

Huw M.L.Davies and Gene H.Lee

Org.Lett, **2004**, *6*, 1233



Erika Englund, Current Lit 4-2004

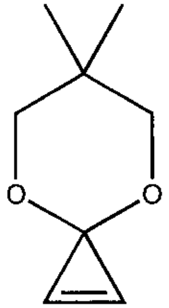
Outline:

- Introduction
- Cyclopropenes in Nature
- Formation of Cyclopropenes
- Cyclopropene Transformations
- Davies' Early Work
- Title Paper
- Conclusions

Introduction

- Cyclopropene

  The highly strained alkene presents a reactive substrate capable of useful transformations such as:
  - Diels-Alder
  - Grignard Additions
  - Vinyl Carbene Formation

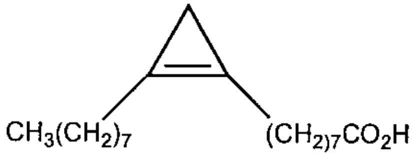


- Cyclopropene Acetal
  - First described in literature in 1959
  - In the mid 1980's, Boger began to incorporate this functionality into several total syntheses of natural products
  - Nakamura and others have contributed to a growing body of work concerning methodology and synthetic potential

CPA Review: Chem Rev. **2003**, *103*, 1295

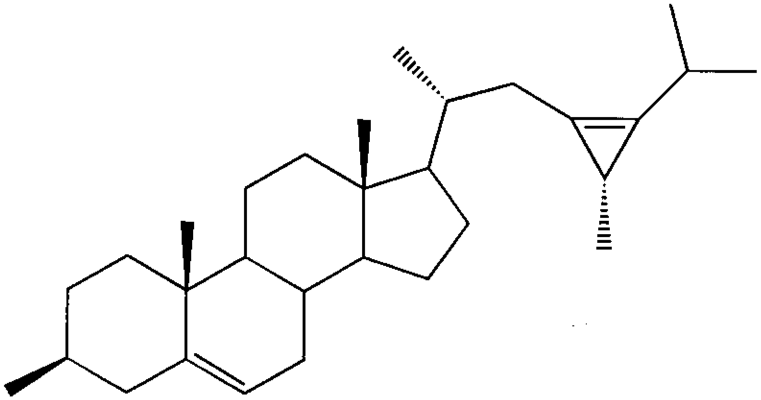
Cyclopropenes in Nature

- Sterculic Acid (inhibitor of Δ9-desaturase)



Tet.Lett, **1992**, *33*, 1521

- Steroid isolated from Calyx Podatypa Sponge

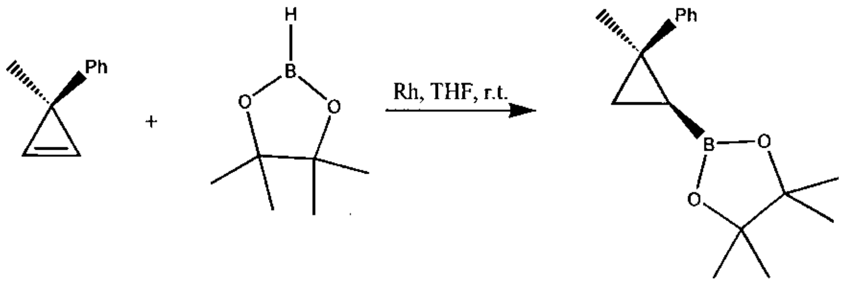


J.A.C.S. **1988**, *110*, 8123

Cyclopropene Transformations

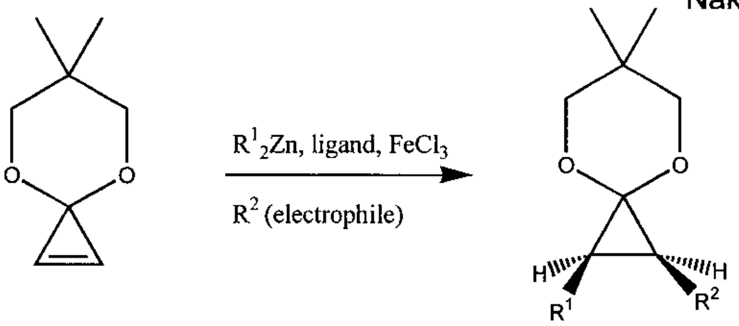
- Enantioselective Hydroboration

Gevorgyan, J.A.C.S. **2003**, *125*, 7198



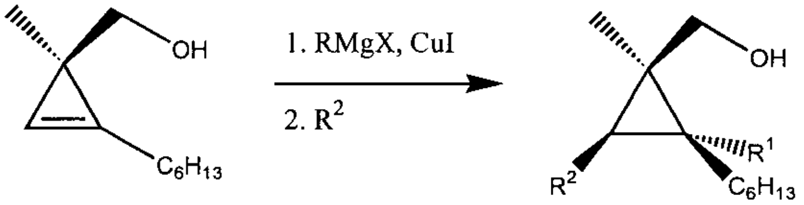
- Iron Catalyzed Olefin Carbometalation

Nakamura, J.A.C.S. **2000**, *122*,978



- Copper Catalyzed Addition of Grignards

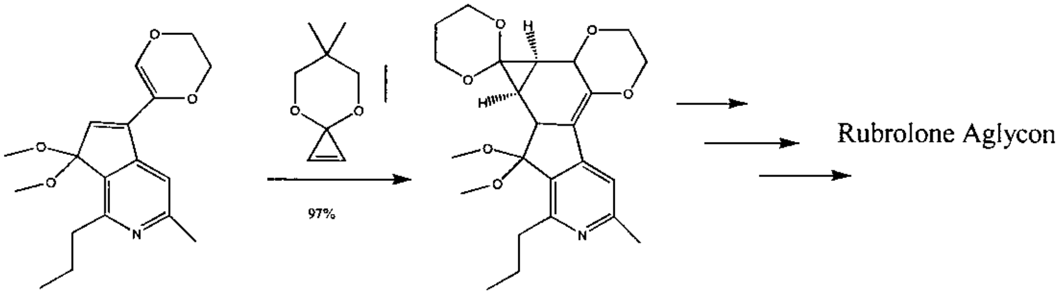
Fox, J.A.C.S. **2002**, *124*, 14322



Cyclopropene Transformations (cont.)

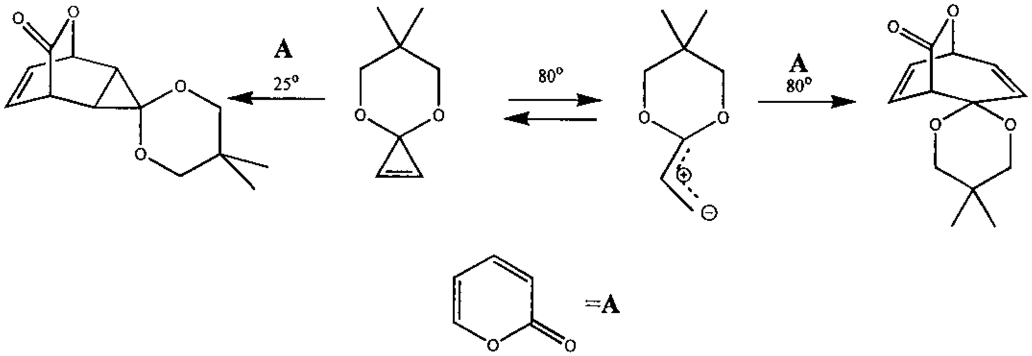
- Diels-Alder

Boger, J.A.C.S. **2000**, *122*, 12169



- Vinyl Carbene Formation

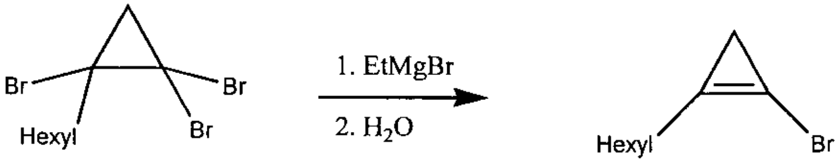
Boger, J.A.C.S. **1995**, *117*, 12452



Formation of Cyclopropenes

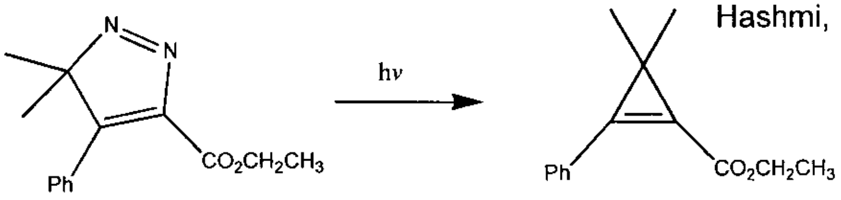
- Basic Conditions

Baird, Tetrahedron, **2002**, *58*, 1581



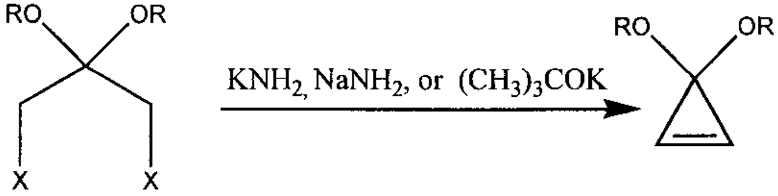
- Photochemically

Hashmi, Eur.J.Org.Chem, **2001**, 4705

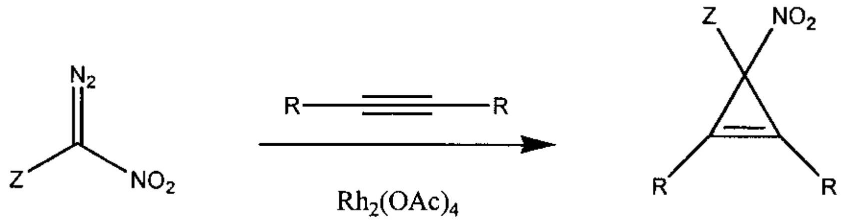


- Cyclopropenone Acetal Formation

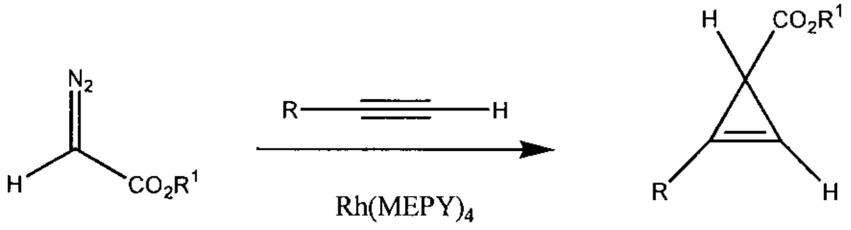
Nakamura, J.O.C. **1989**, *54*, 4727



Cyclopropenation of Alkynes by Diazocompounds



Dailey, J.O.C. **1991**, *56*, 2258



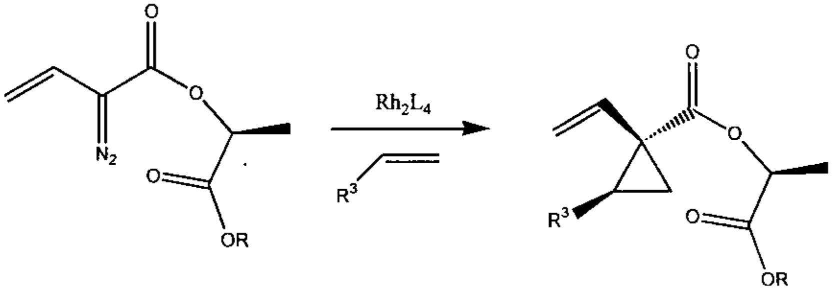
Doyle, J.A.C.S. **1994**, *116*, 8492

The enantioselective cyclopropenation of alkynes is still at a relatively early stage In development. The scope of potential substrates is still being investigated.

Early Work by Davies

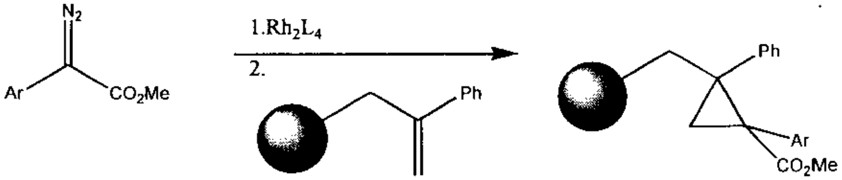
- Asymmetric cyclopropanations with α-hydroxy ester chiral auxiliaries

  J.A.C.S. **1993**, *115*, 9468



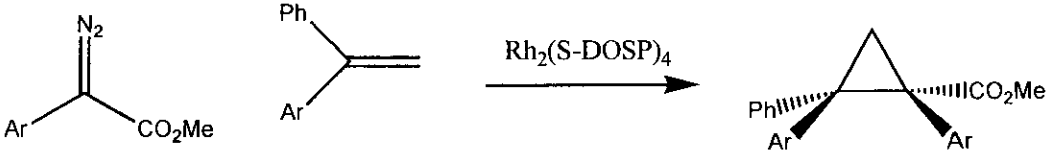
- Catalytic asymmetric solid phase cyclopropanation

  J.A.C.S. **2001**, *123*, 2695

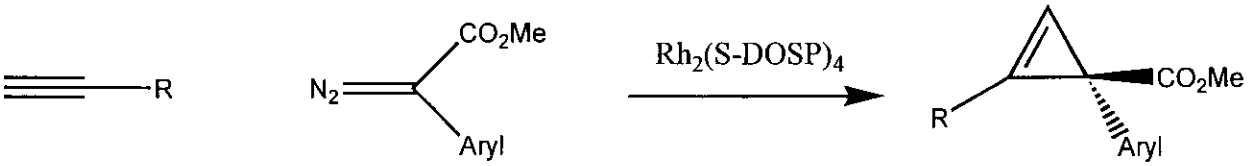


- Rhodium catalyzed asymmetric cyclopropanations

  Org.Let, **2000**, *6*, 823

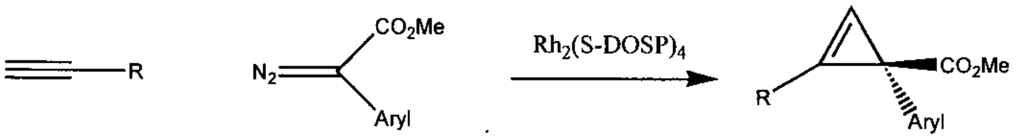


Title Paper:

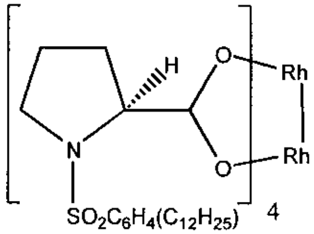


- Goals:
  - Cyclopropenate alkynes with aryl diazoacetates (a more stabilized carbenoid than diazoacetates)
  - Enantioselectively form a new quartenary center

Reaction Conditions:

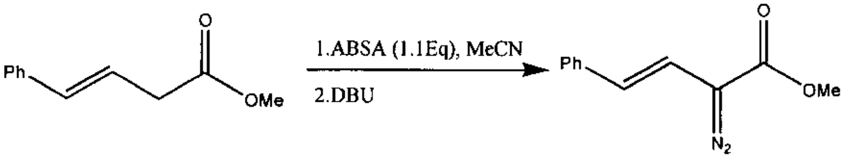


$Rh_2(S\text{-}DOSP)_4$=



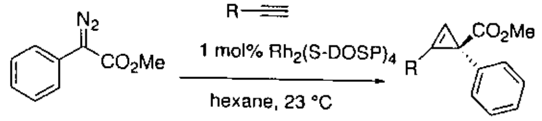
- 1 mol% of the rhodium catalyst and 10 eq of alkyne were stirred at r.t. in hexanes. The diazo compound was added over the course of 5 hours

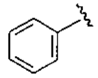
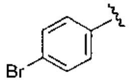
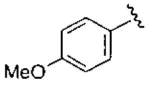
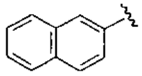
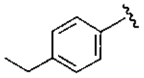
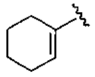
- Formation of Diazo Compounds (ex.)



Scope of Alkynes

Table 1. $Rh_2(S\text{-DOSP})_4$-Catalyzed Enantioselective Cylopropenation with Methyl Phenyldiazoacetate[a]



entry	R	product	yield, %	ee, %
1		2	62	90
2		3	63	92
3		4	67	86
4		5	60	96
5		6	48	87
6		7	74	92
7	$(CH_2)_3CH_3$	8	51	84

[a] Reactions were performed by the addition of the diazo compound (1.0 mmol) in 5 mL of hexanes over a 5-h period to a solution of the alkyne (10.0 mmol) and catalyst (0.01 mmol) in 10 mL of hexanes. See the Supporting Information for details.

- Conclusions
  - Cyclopropenation occurs prior to C-H bond insertion
  - Cyclopropenation occurs prior to cyclopropanation
  - Cyclopropenation occurs with hexyne with a small drop in ee and yield

Scope of Diazo Acetates

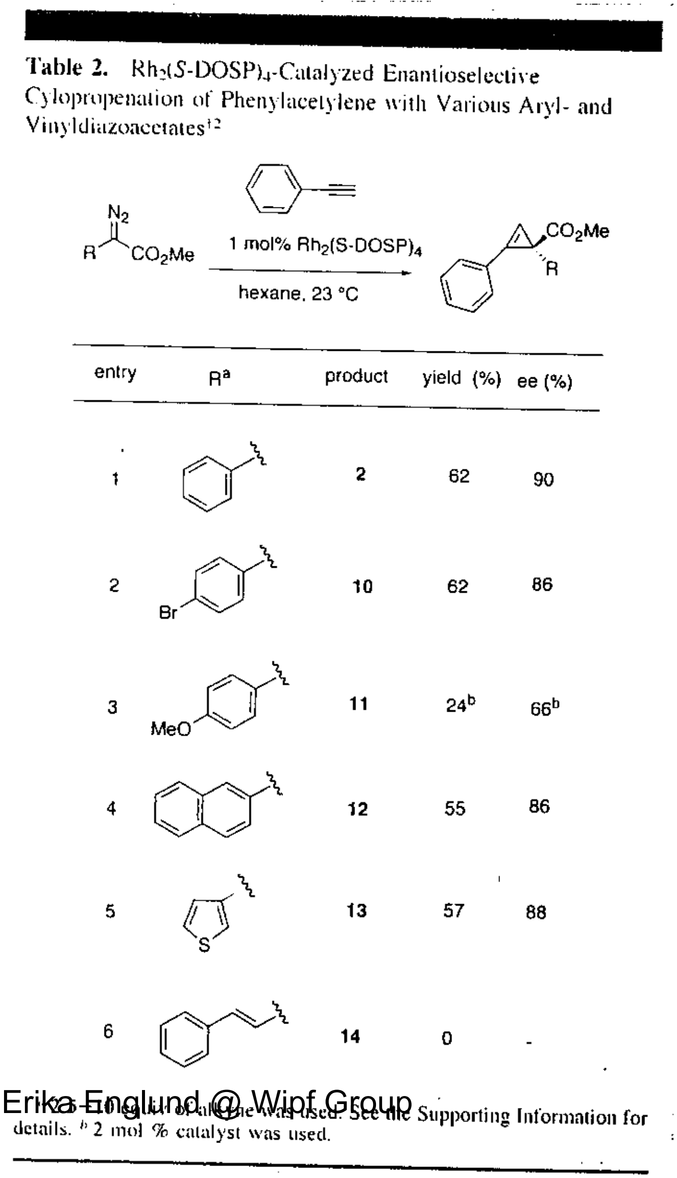


Table 2. Rh_2(*S*-DOSP$)_4$-Catalyzed Enantioselective Cylopropenation of Phenylacetylene with Various Aryl- and Vinyldiazoacetates[12]

entry	R[a]	product	yield (%)	ee (%)
1		2	62	90
2	Br	10	62	86
3	MeO	11	24[b]	66[b]
4		12	55	86
5	S	13	57	88
6		14	0	-

[a] 2.5–10 equiv of alkyne was used. See the Supporting Information for details. [b] 2 mol % catalyst was used.

- Conclusions
  - Moderate yield and ee's
  - P-methoxy derivative gave the lowest yield (potentially due to reduced reactivity of carbenoid)
  - Styryl diazoacetate gave no reaction (possibly due to an unstable product?)

Kinetic Studies

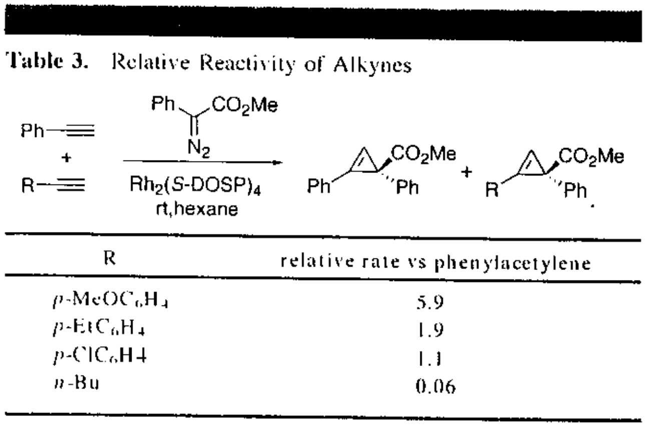


Table 3. Relative Reactivity of Alkynes

R	relative rate vs phenylacetylene
p-$MeOC_6H_4$	5.9
p-EtC_6H_4	1.9
p-ClC_6H_4	1.1
n-Bu	0.06

- Conclusions
  - The most reactive substrates are the most electron rich
    - This is indicative of a positive charge buildup at the benzylic carbon at the transition state
  - This is a similar result as the results from the kinetic studies of cyclopropanation

Mechanistic Studies

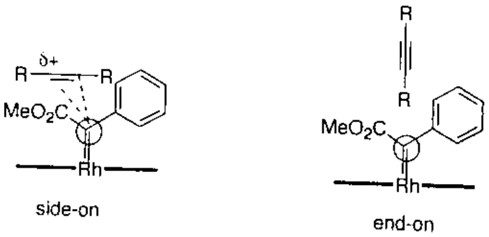


Figure 1. Comparison of side-on[7] and end-on[14] approaches for cyclopropenation.

- In 1996, the cyclopropanation of alkenes were proposed to go through the side-on trajectory. If the cyclopropenation of alkynes also went through a side-on trajectory, it should be possible to cylopropenate internal alkynes
  - This was tested with 1-phenyl-1-propyne. There was no observed reaction
  - When Doyle tested this alkyne with the diazo acetate he reported 39% yield and 16%ee

Diazo acetates are classified as "unstabilized carbenoids" (they lack the donor and acceptor groups that the aryl diazoacetates have). This leads to greater reactivity

Tetrahedron, **2000**, *56*, 4880

Davies' Conclusions

- Rhodium Catalyzed cyclopropenation can act as an efficient catalyst for both cyclopropenations and cyclopropanations
- Aryl diazoacetates can react enantioselectively in the presence of the rhodium catalyst to provide cyclopropenes containing a quartenary center
- This work expands the range of chiral cyclopropenes that can be used as synthetic building blocks

Conclusions

- Since the work by Boger in the 1980's, there has been an increase in attention to the potential of cyclopropenes and cyclopropenone acetals in synthesis
- As of recently, cyclopropenone acetals have been the more common cyclopropene variant used in synthesis
- With the work of Davies and others, the variety of chiral cyclopropenes is expanding. With the greater variety, the potential for synthetic applications is also increasing