

# CYCLOADDITION REACTIONS OF VINYL CARBENOIDS

Reporter: Zhang-Pei Chen

Checker : Mu-Wang Chen

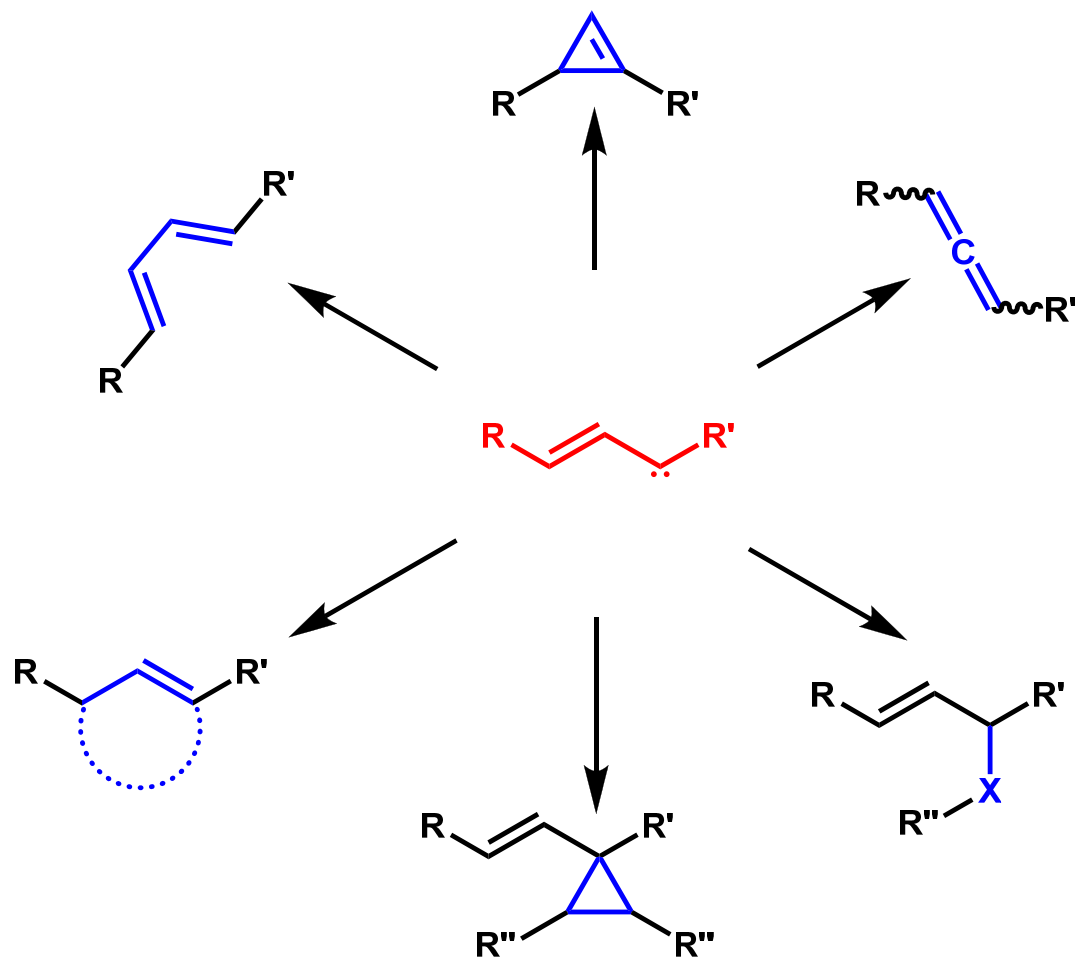
Date: 16/12/2014

Davies, H. M. L. *et al.*  
*Angew. Chem. Int. Ed.* **2014**, 53, 13083 .

# Free vinyl carbenes

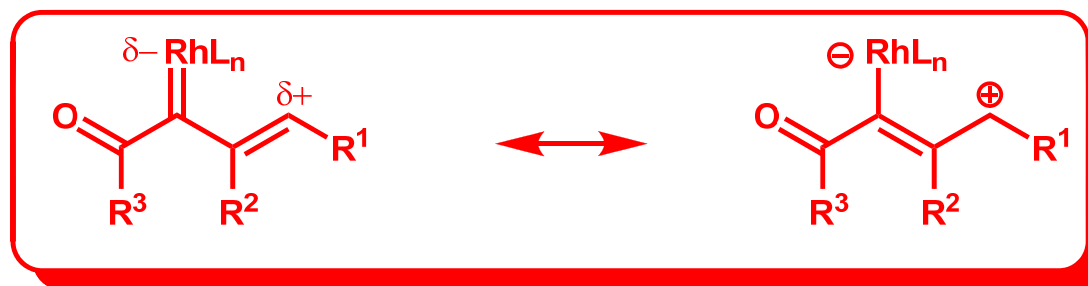
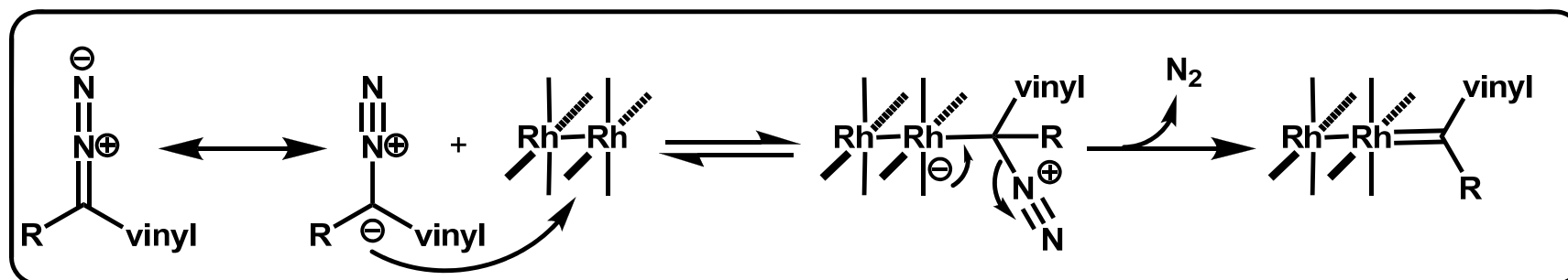
---

The chemistry of vinyl carbenes is dominated by their propensity for intramolecular reactions. When appropriately functionalized, they can undergo rearrangements to cyclopropenes, allenes, acetylenes and dienes, insertion onto C-H, O-H and C=C bonds.



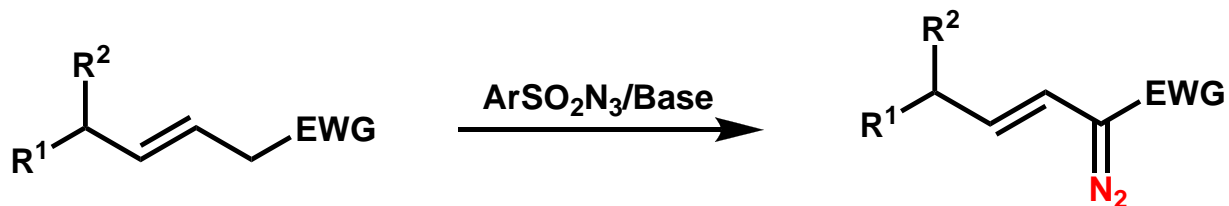
# Carbenoid formation from diazo compounds

The reactivity of vinyl carbenes might be quite different if they were generated by metal catalyzed decomposition of vinyl diazo compounds. Under these conditions the intermediate would be a metal carbenoid complex which should be more stable than the free carbene. Undesirable intramolecular reactions, therefore, should be more controllable.

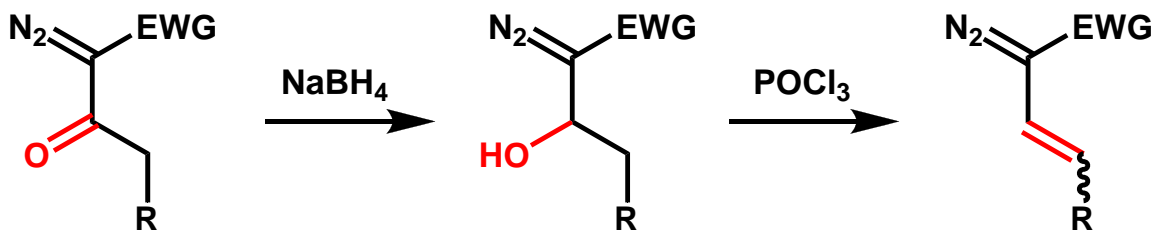
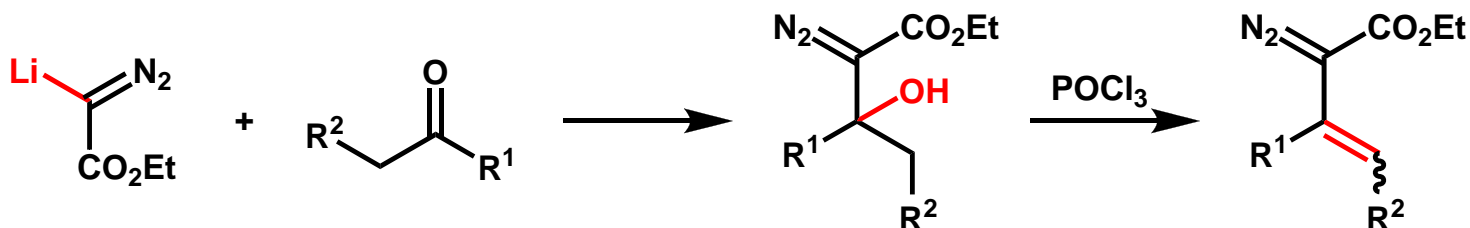


# Synthesis of vinyldiazomethanes

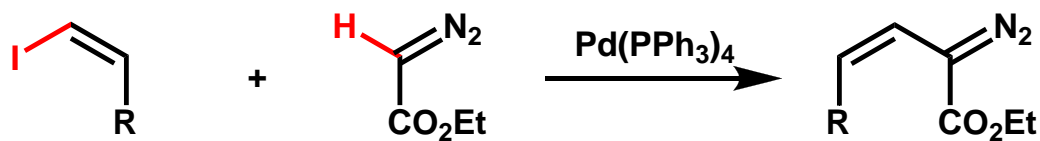
## a) Base induced elimination of tosylhydrazones



## b) Elimination of *ortho*-hydroxyl-diazocompounds

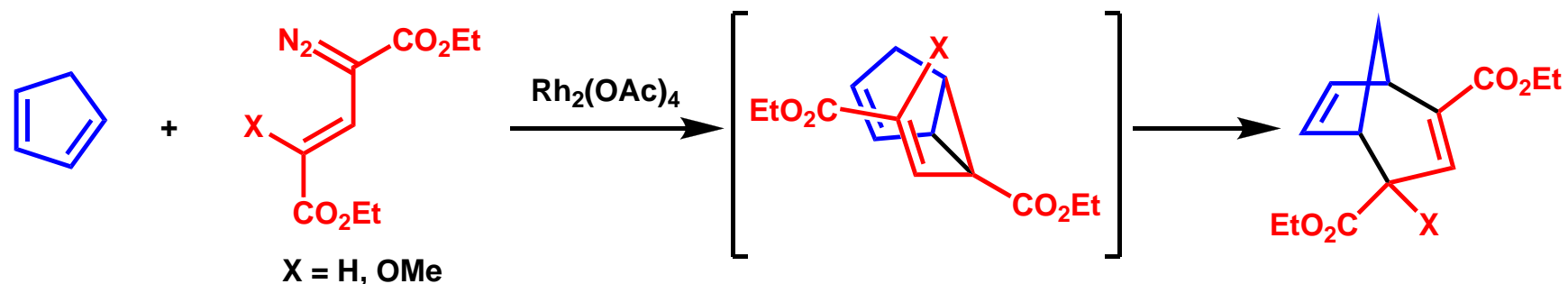


## c) Coupling reactions

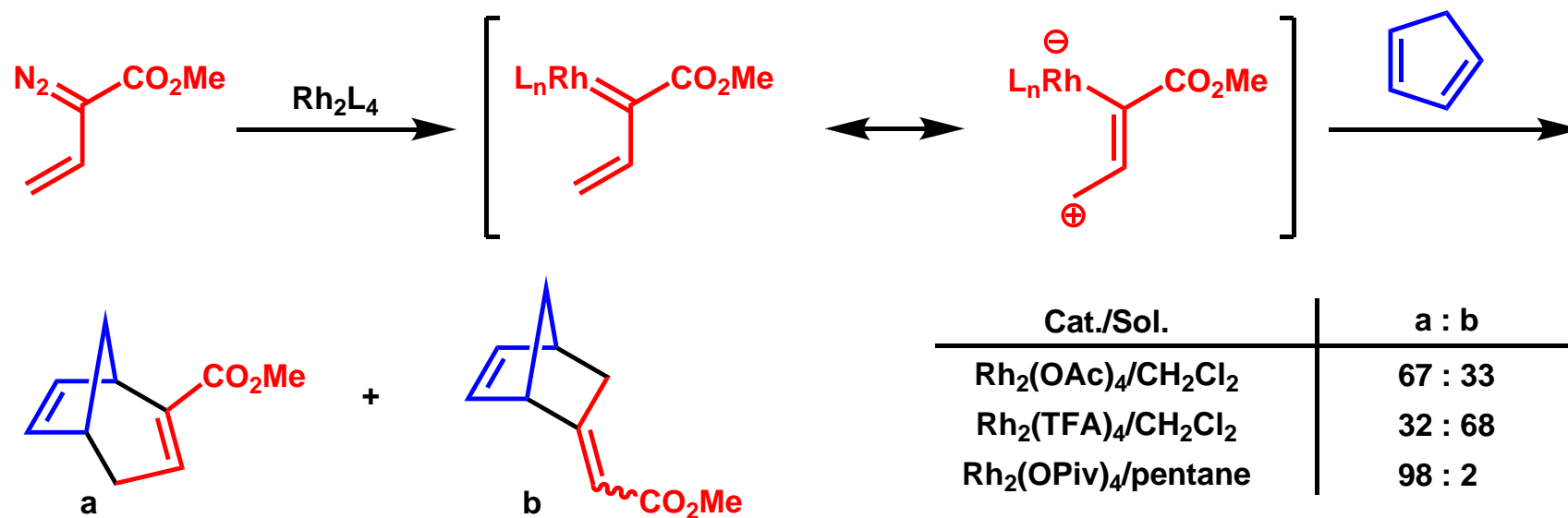


# Reaction with dienes

## Tandem cyclopropanation/Cope rearrangement

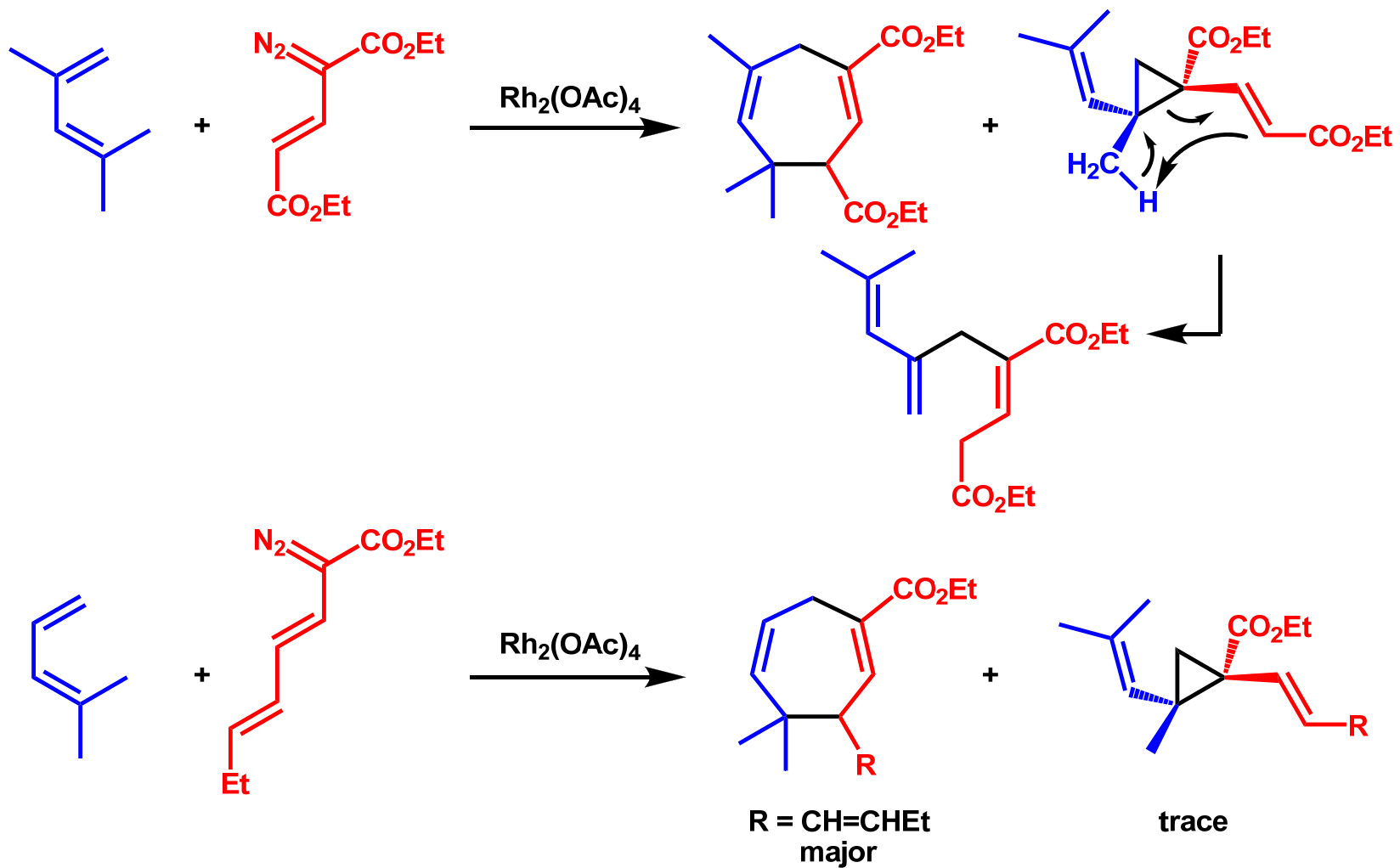


Davies, H. M. L. *et al. Tetrahedron Lett.* **1987**, 28, 1853.

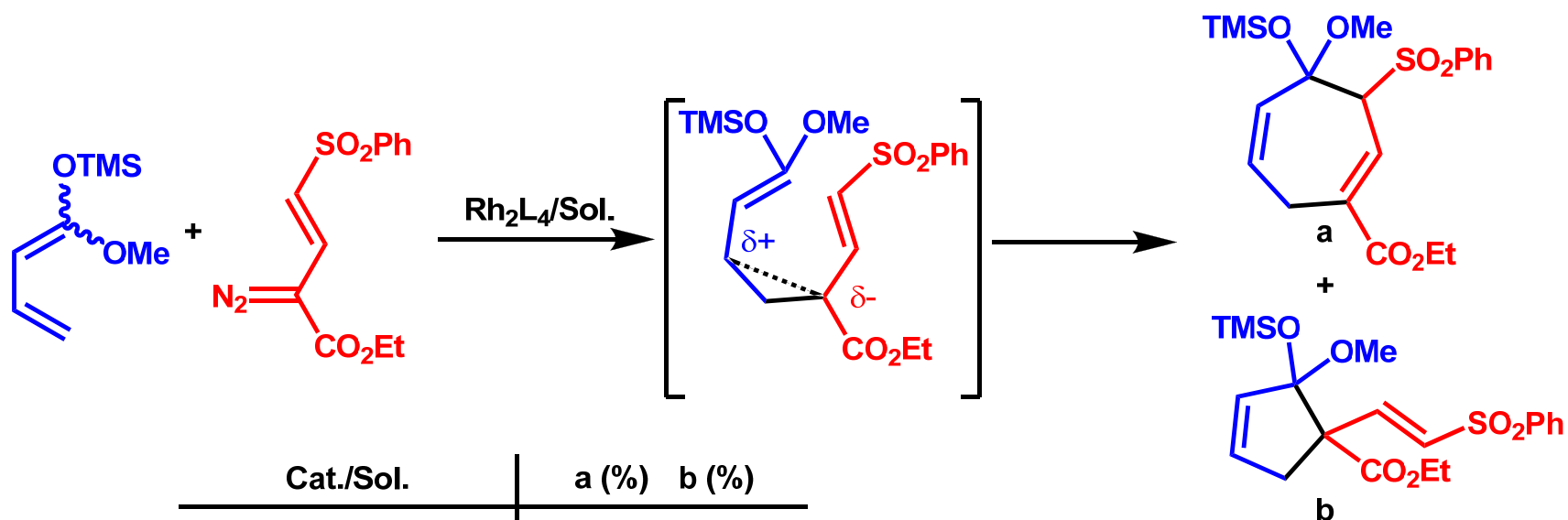
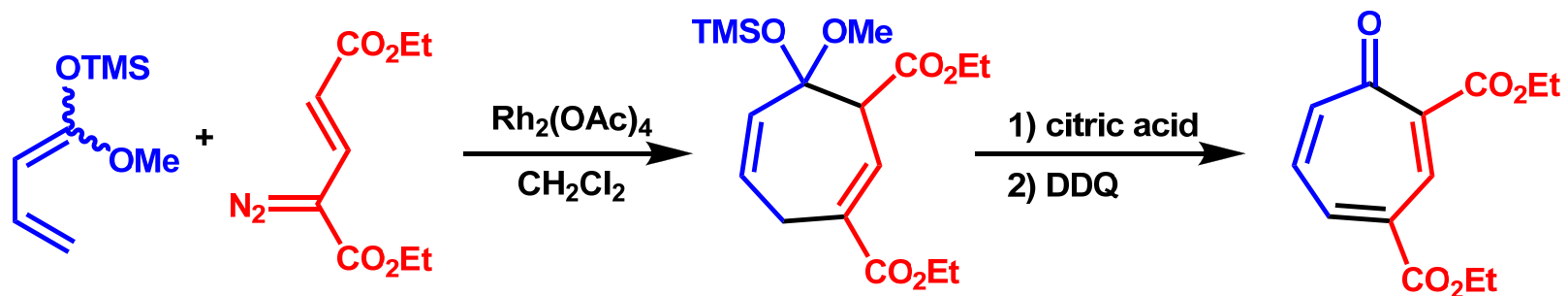


Davies, H. M. L. *et al. Tetrahedron Lett.* **1990**, 31, 6299.

# Reaction with dienes

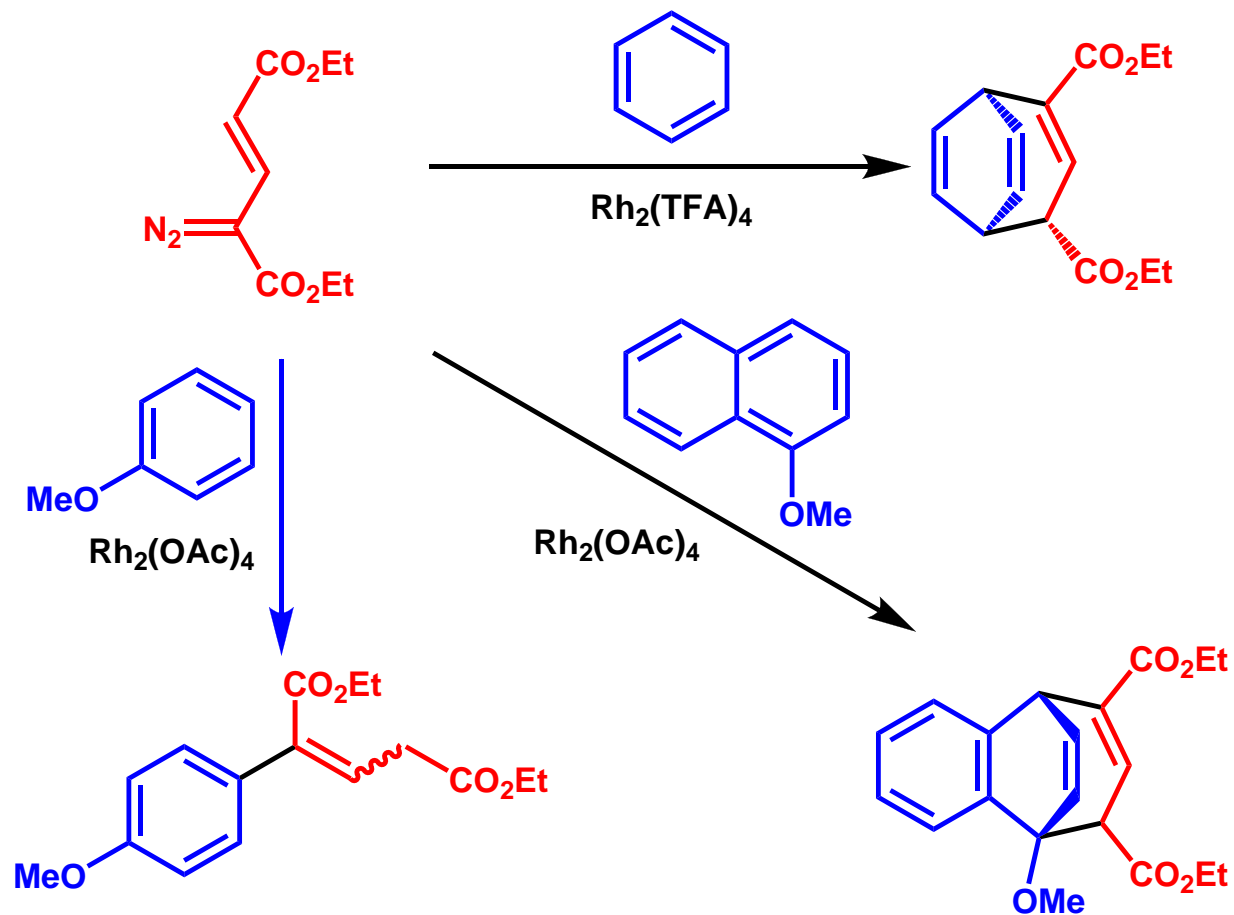


# Reaction with oxygenated dienes



Cat./Sol.	a (%)	b (%)
Rh <sub>2</sub> (OAc) <sub>4</sub> /CH <sub>2</sub> Cl <sub>2</sub>	23	47
Rh <sub>2</sub> (OPiv) <sub>4</sub> /pentane	79	0

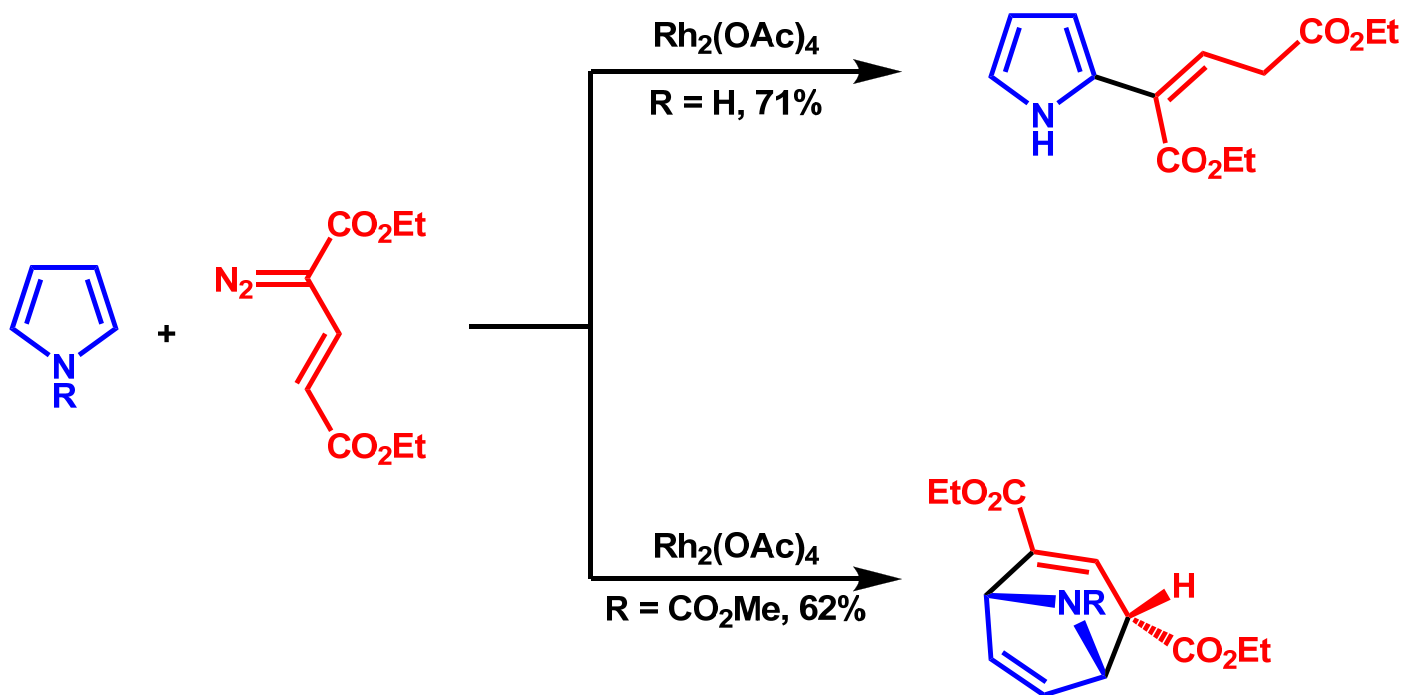
# Reaction with aromatic systems



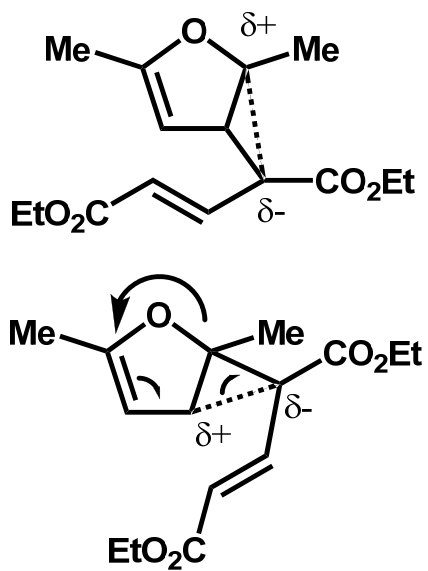
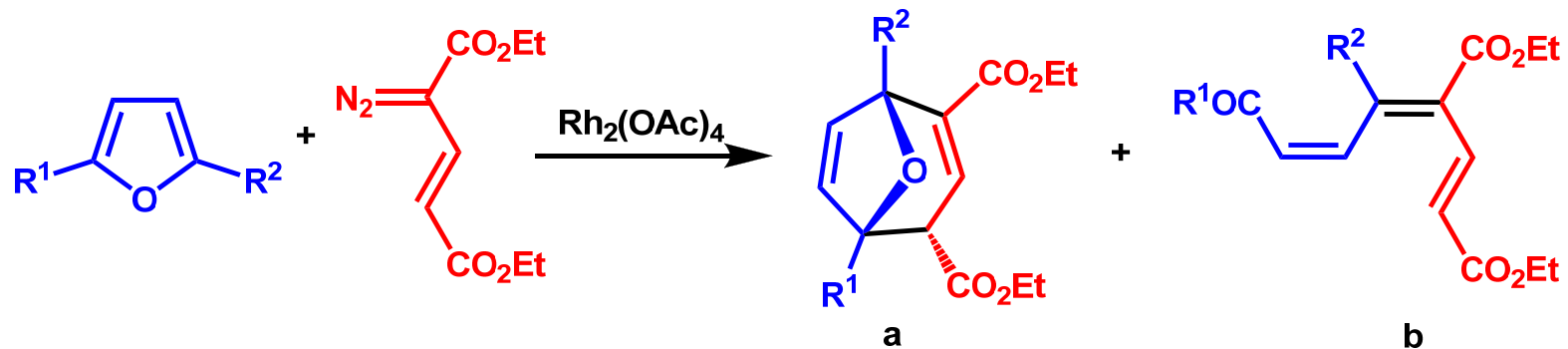


# Reaction with aromatic systems

---

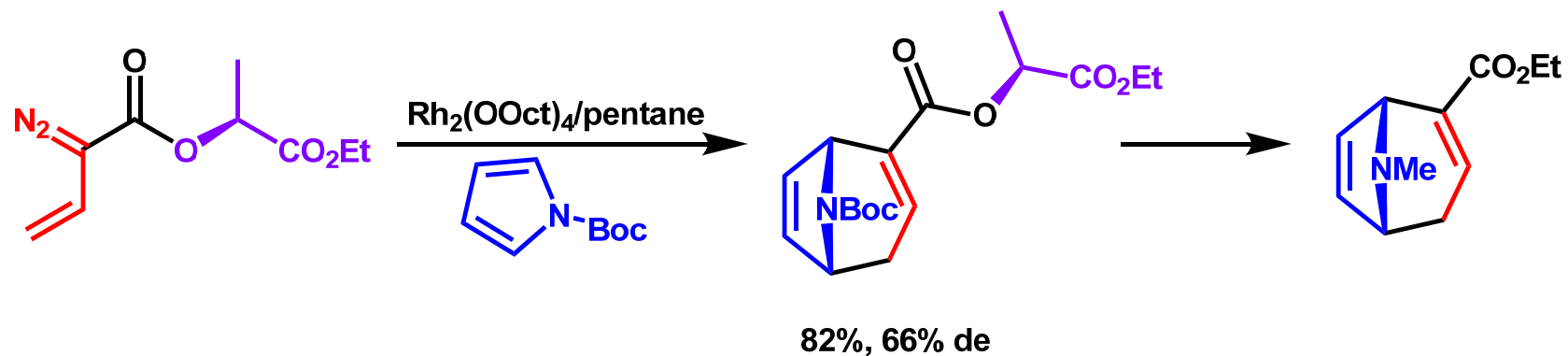
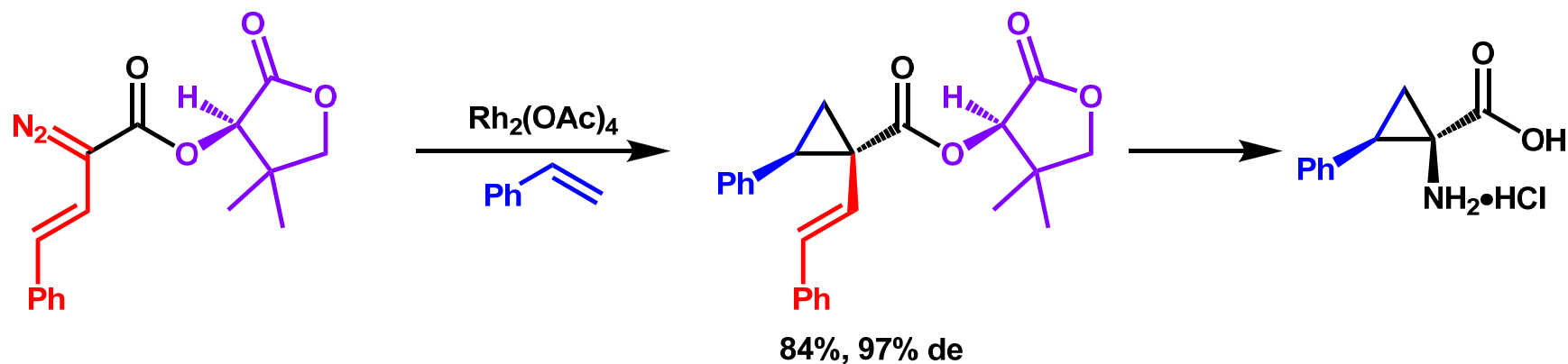


# Reaction with aromatic systems



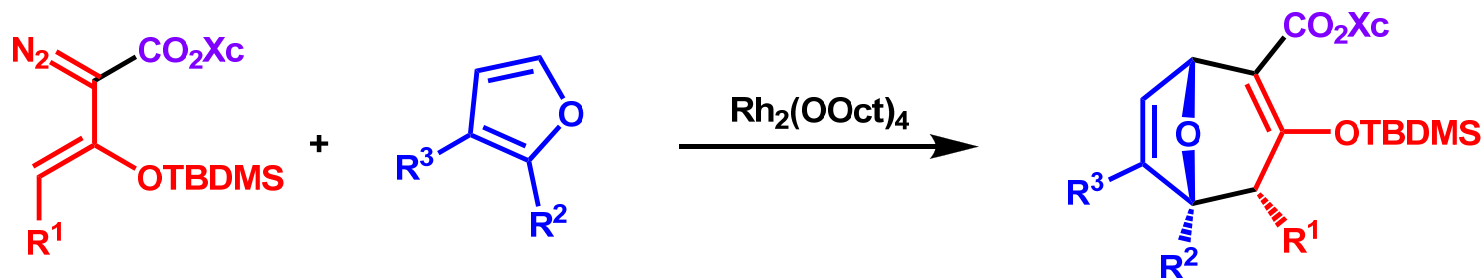
$R^1$	$R^2$	a (%)	b (%)
H	H	62	26
Me	H	8	74
OMe	H	0	92
Me	Me	70	0

# Asymmetric reactions of vinylcarbenoids



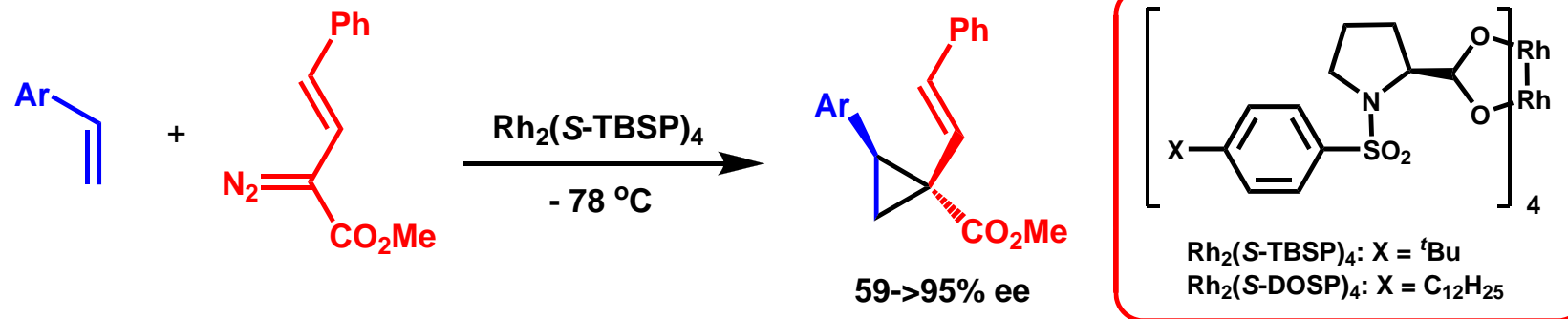
Davies, H. M. L. *et al. Tetrahedron Lett.* **1991**, 32, 6509.  
Davies, H. M. L. *et al. Tetrahedron Lett.* **1992**, 33, 6935.

# Asymmetric reactions of vinylcarbenoids

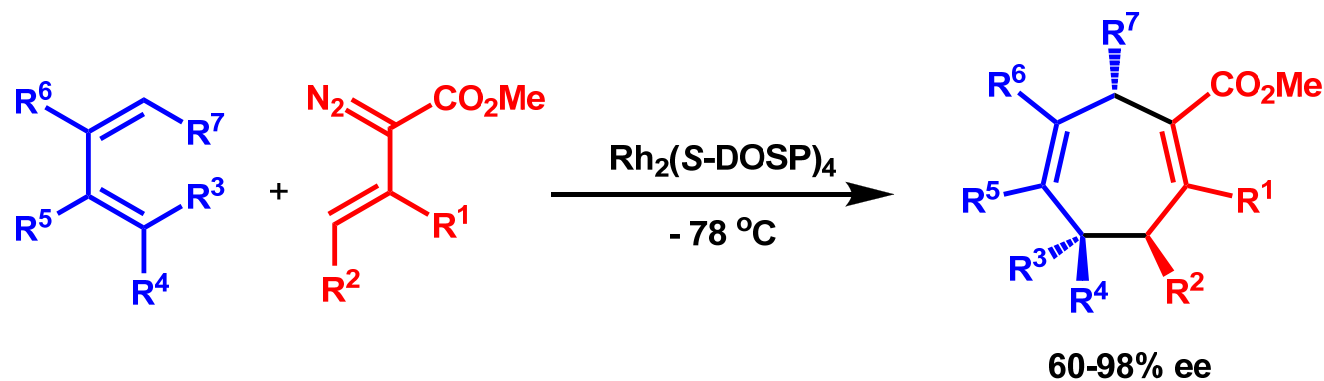


Xc	$\text{R}_1$	$\text{R}_2$	$\text{R}_3$	Yield (%)	de (%)
(S)-lactate	H	H	H	72	79
(R)-pantolactone	H	H	H	82	94
(S)-lactate	Me	H	H	62	90
(R)-pantolactone	Me	H	H	75	95
(S)-lactate	H	Me	H	81	75
(R)-pantolactone	H	Me	H	91	83
(S)-lactate	Me	Me	H	91	84
(R)-pantolactone	H	Me	$\text{CO}_2\text{Me}$	65	82

# Asymmetric reactions of vinylcarbenoids

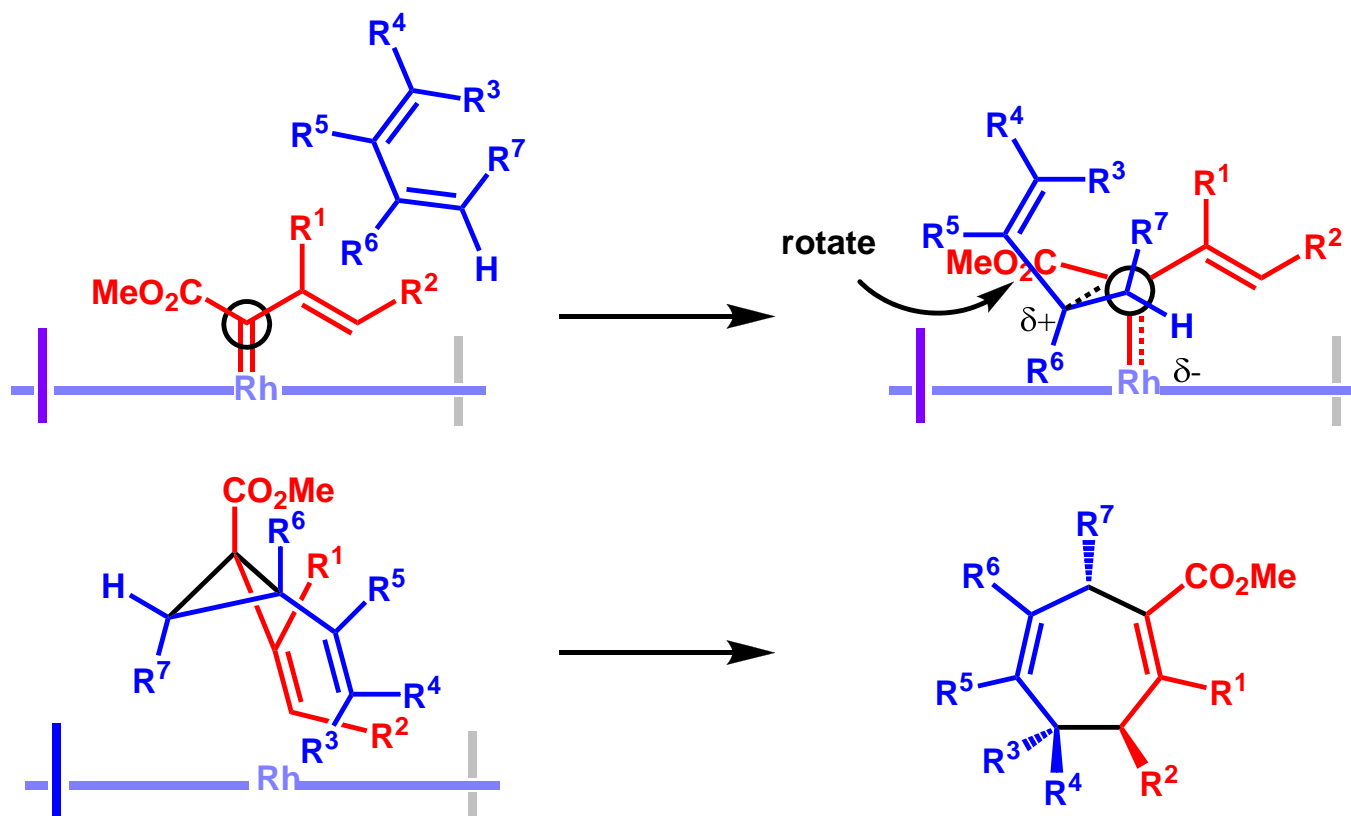


Davies, H. M. L. *et al. Tetrahedron Lett.* **1993**, 34, 7243.

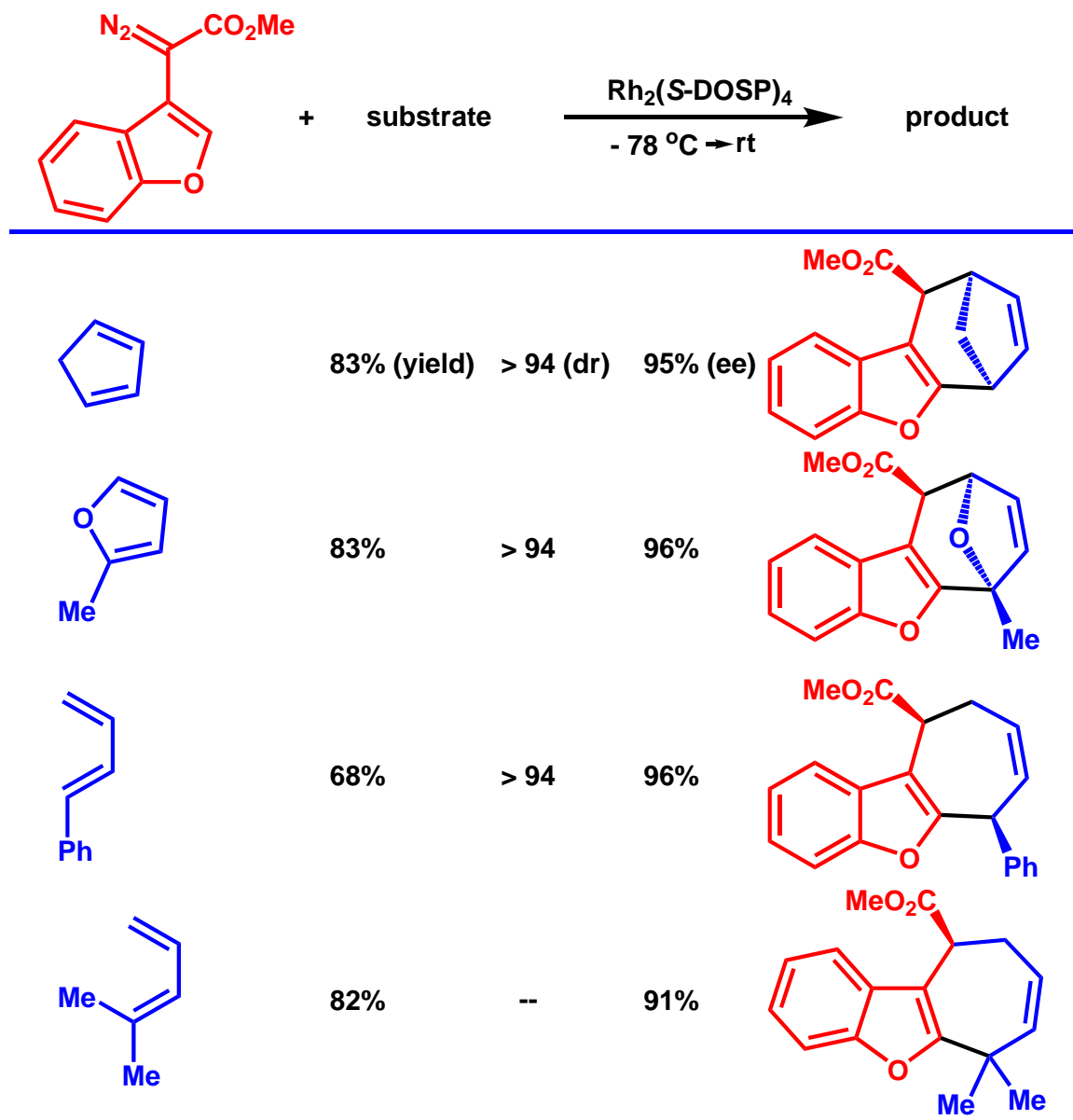


Davies, H. M. L. *et al. J. Am. Chem. Soc.* **1998**, 120, 3326.

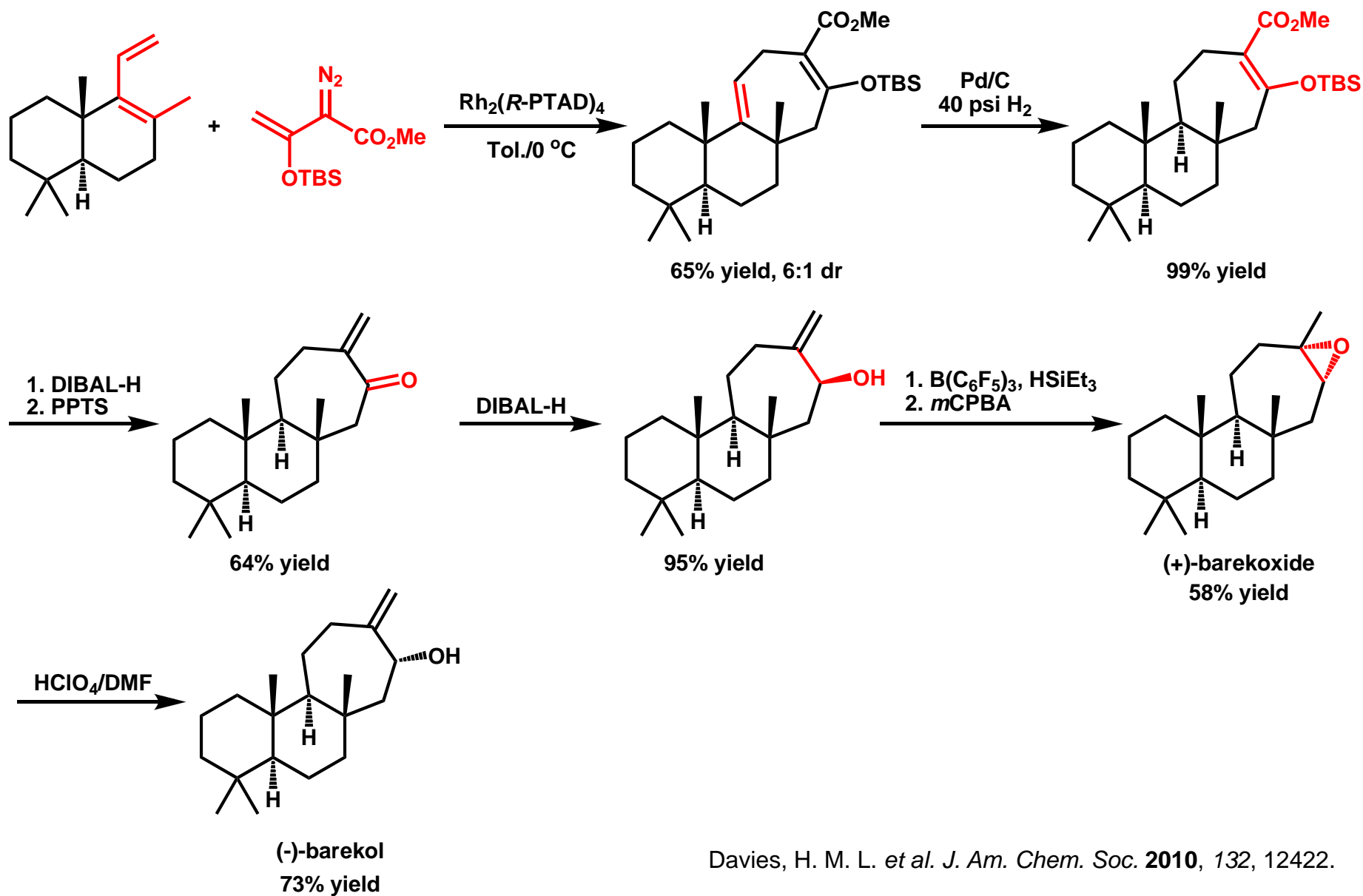
# Asymmetric reactions of vinylcarbenoids



# Asymmetric reactions of vinylcarbenoids



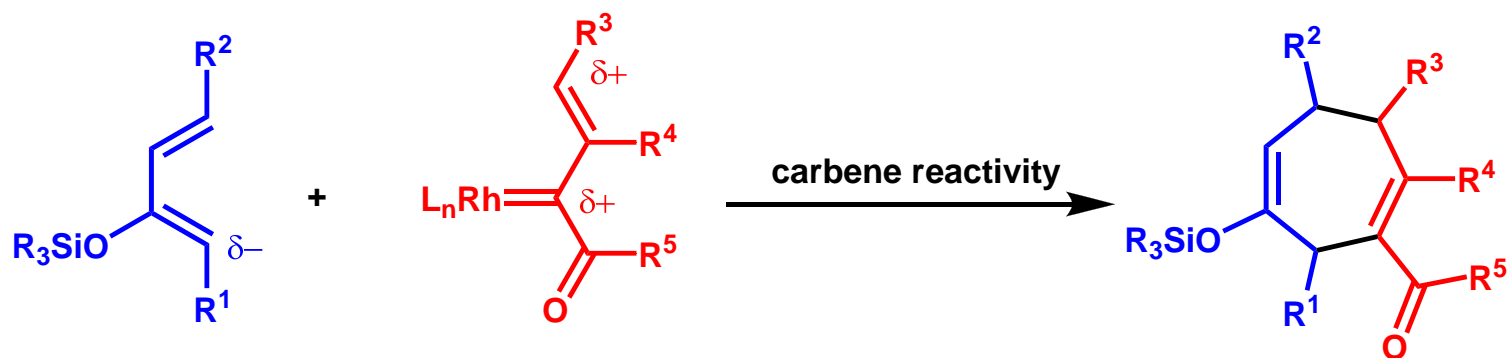
# Asymmetric reactions of vinylcarbenoids



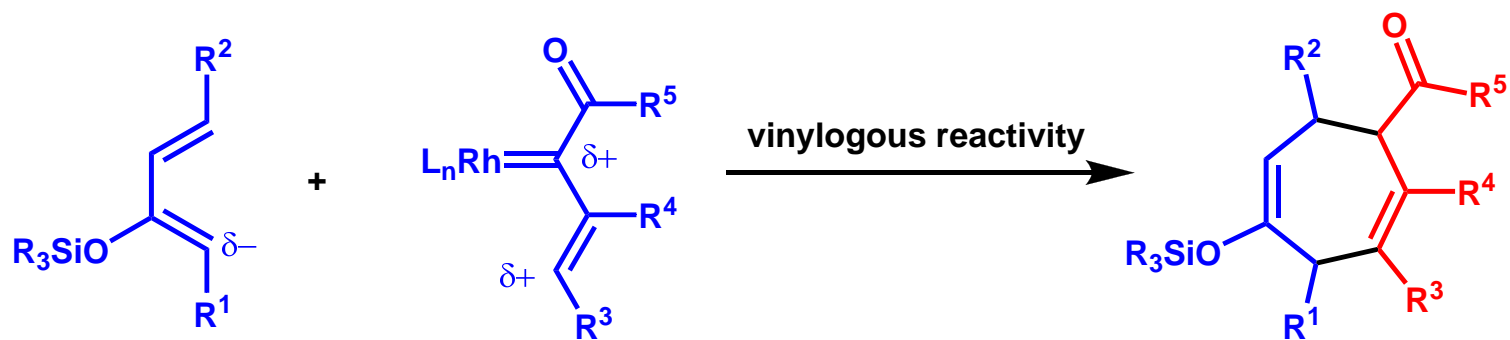


# Asymmetric reactions of vinylcarbenoids

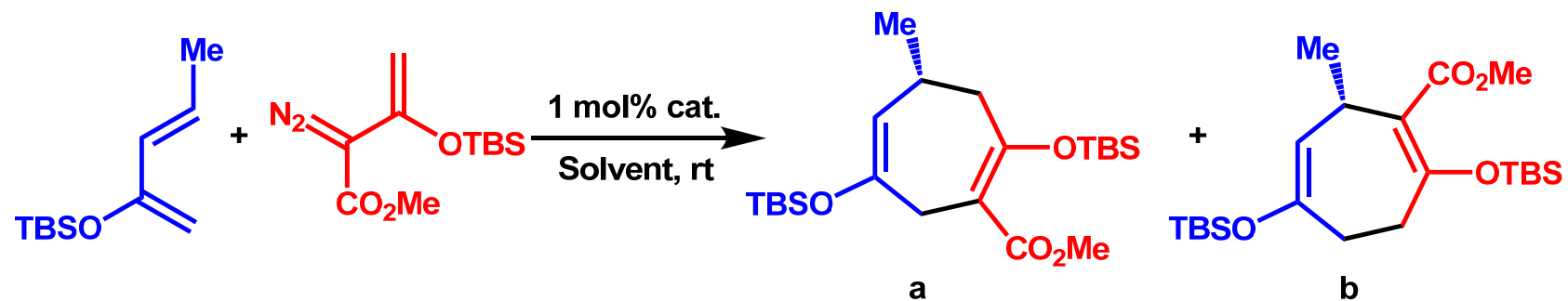
## a) Tandem cyclopropanation/Cope rearrangement



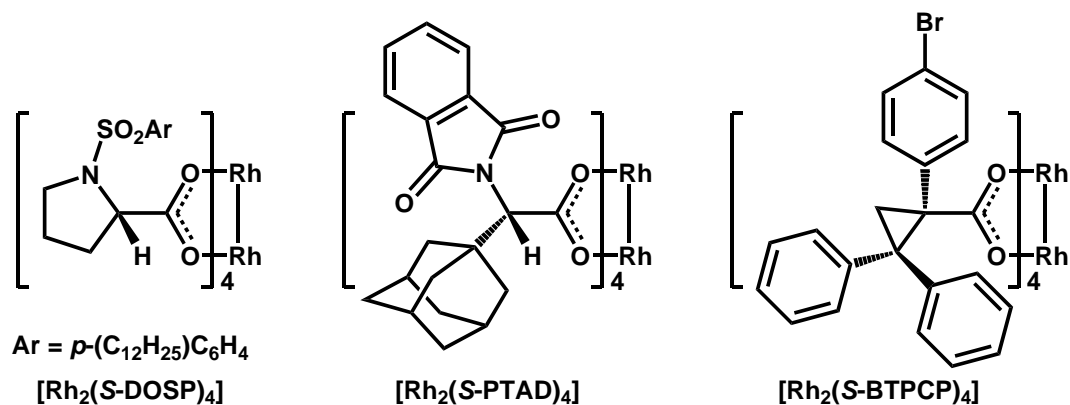
## b) [4+3] Cycloaddition with reverse regiocontrol



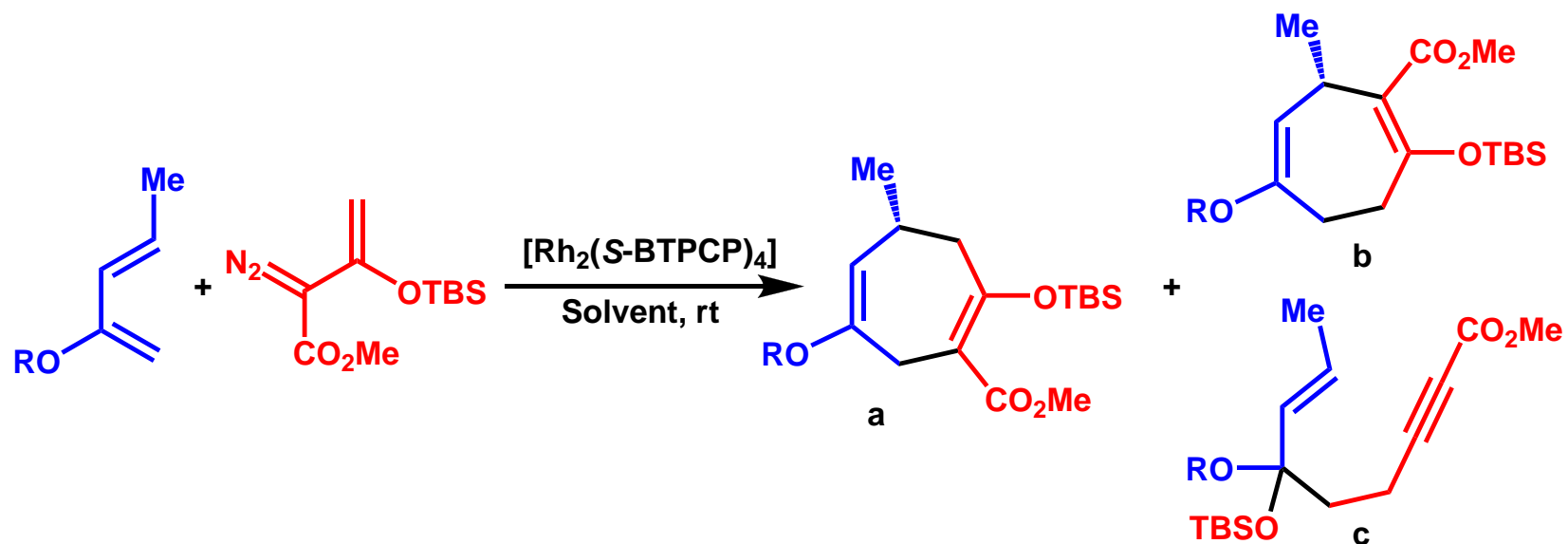
# Asymmetric reactions of vinylcarbenoids



Entry	Solvent	Cat.	a/b	Yield (a+b)	ee of <b>b</b> (%)
1	pentane	[Rh <sub>2</sub> (S-PTAD) <sub>4</sub> ]	94:6	55% ( <b>a</b> )	-73
2	CH <sub>2</sub> Cl <sub>2</sub>	[Rh <sub>2</sub> (S-PTAD) <sub>4</sub> ]	87:13	43%	-71
3	pentane	[Rh <sub>2</sub> (S-DOSP) <sub>4</sub> ]	79:21	62%	33
4	CH <sub>2</sub> Cl <sub>2</sub>	[Rh <sub>2</sub> (S-DOSP) <sub>4</sub> ]	30:70	61%	5

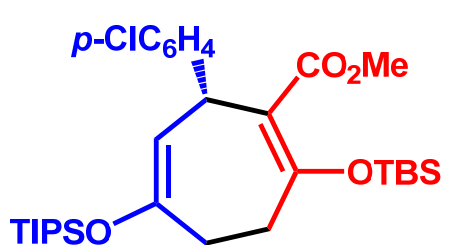
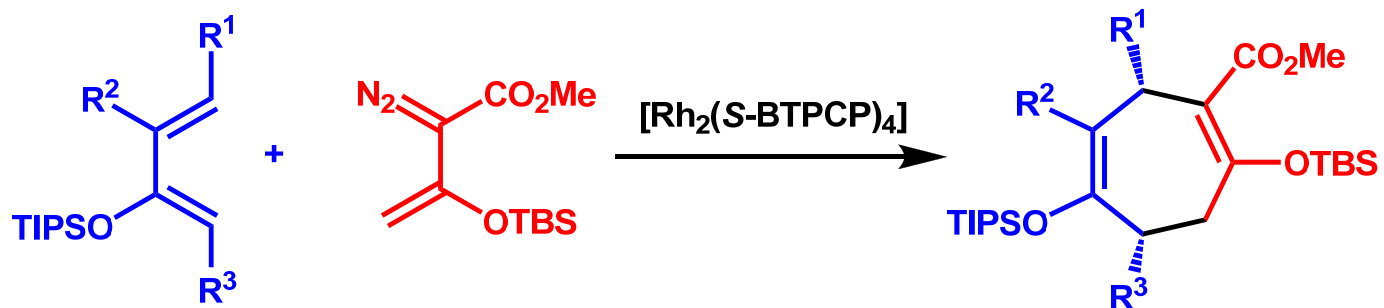


# Asymmetric reactions of vinylcarbenoids

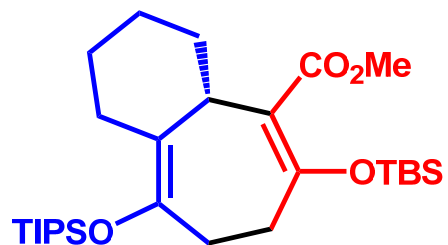


Entry	R	Sol.	<b>a/b/c</b>	Yield (%)	ee of <b>b</b> (%)
1	TBS	CH <sub>2</sub> Cl <sub>2</sub>	9:70:26	37 ( <b>a+b</b> ), 16 ( <b>c</b> )	54
2	TBS	pentane	4:29:62	23 ( <b>a+b</b> ), 42 ( <b>c</b> )	87
3	TMS	pentane	14:18:68	16 ( <b>a+b</b> ), 45 ( <b>c</b> )	70
4	TIPS	pentane	5:95:trace	59 ( <b>b</b> )	96

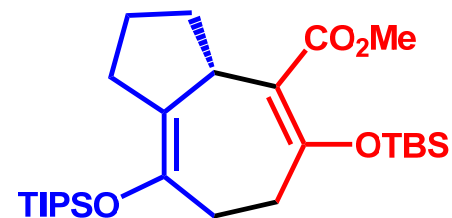
# Asymmetric reactions of vinylcarbenoids



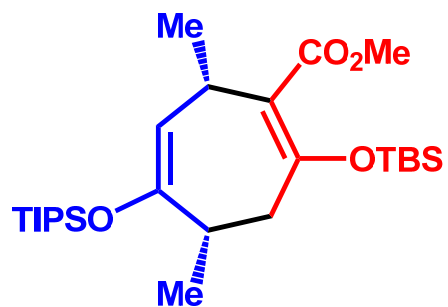
77% yield, 95% ee



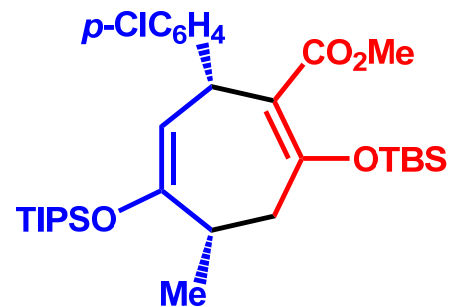
78% yield, 87% ee



65% yield, 82% ee



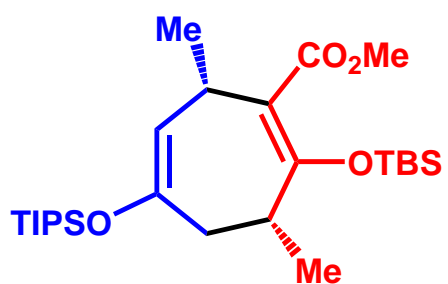
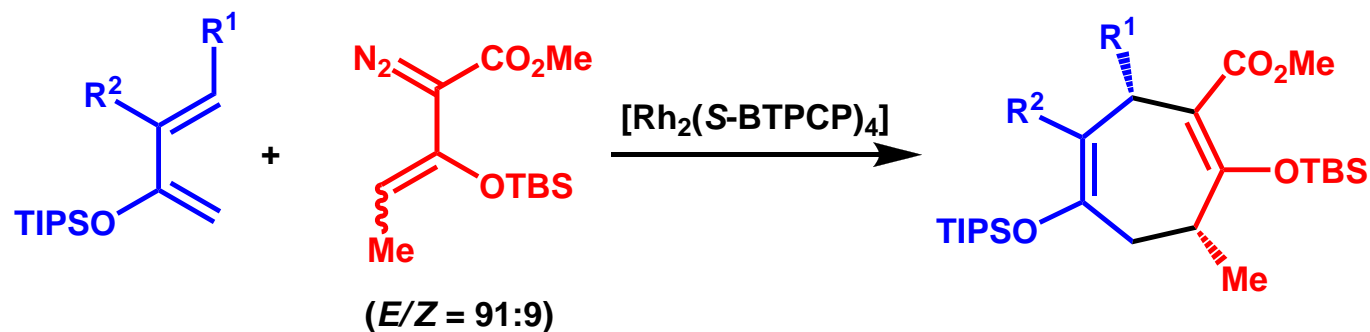
68% yield, 96% ee  
dr > 30:1



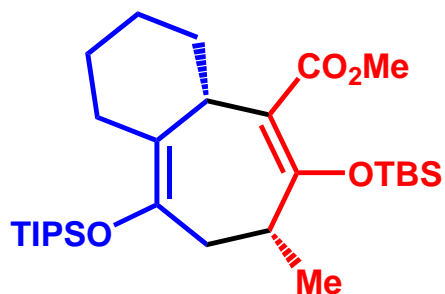
71% yield, 96% ee  
dr > 30:1

# Asymmetric reactions of vinylcarbenoids

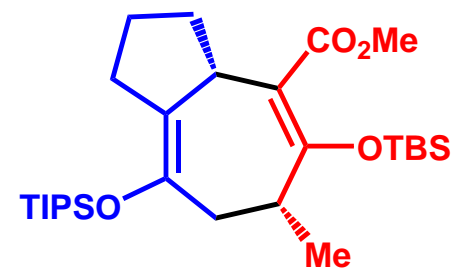
---



59% yield, 99% ee  
dr > 30:1



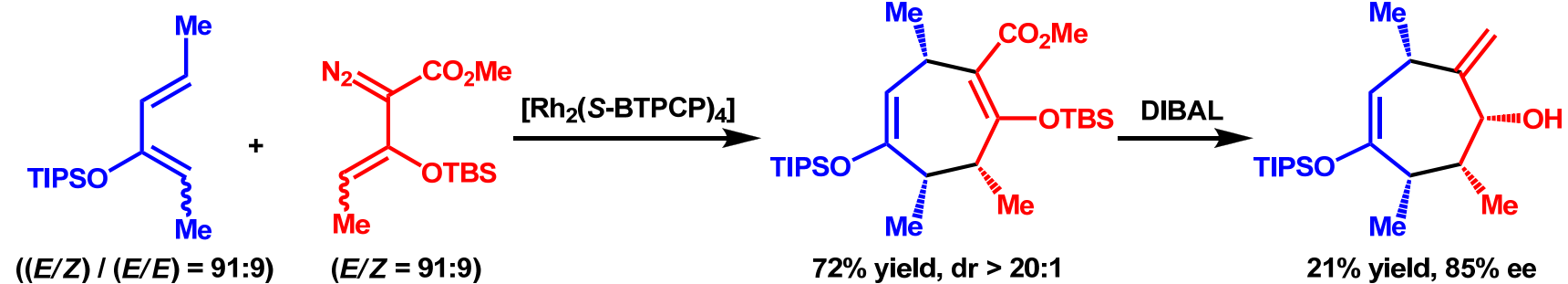
80% yield, 92% ee  
dr > 30:1



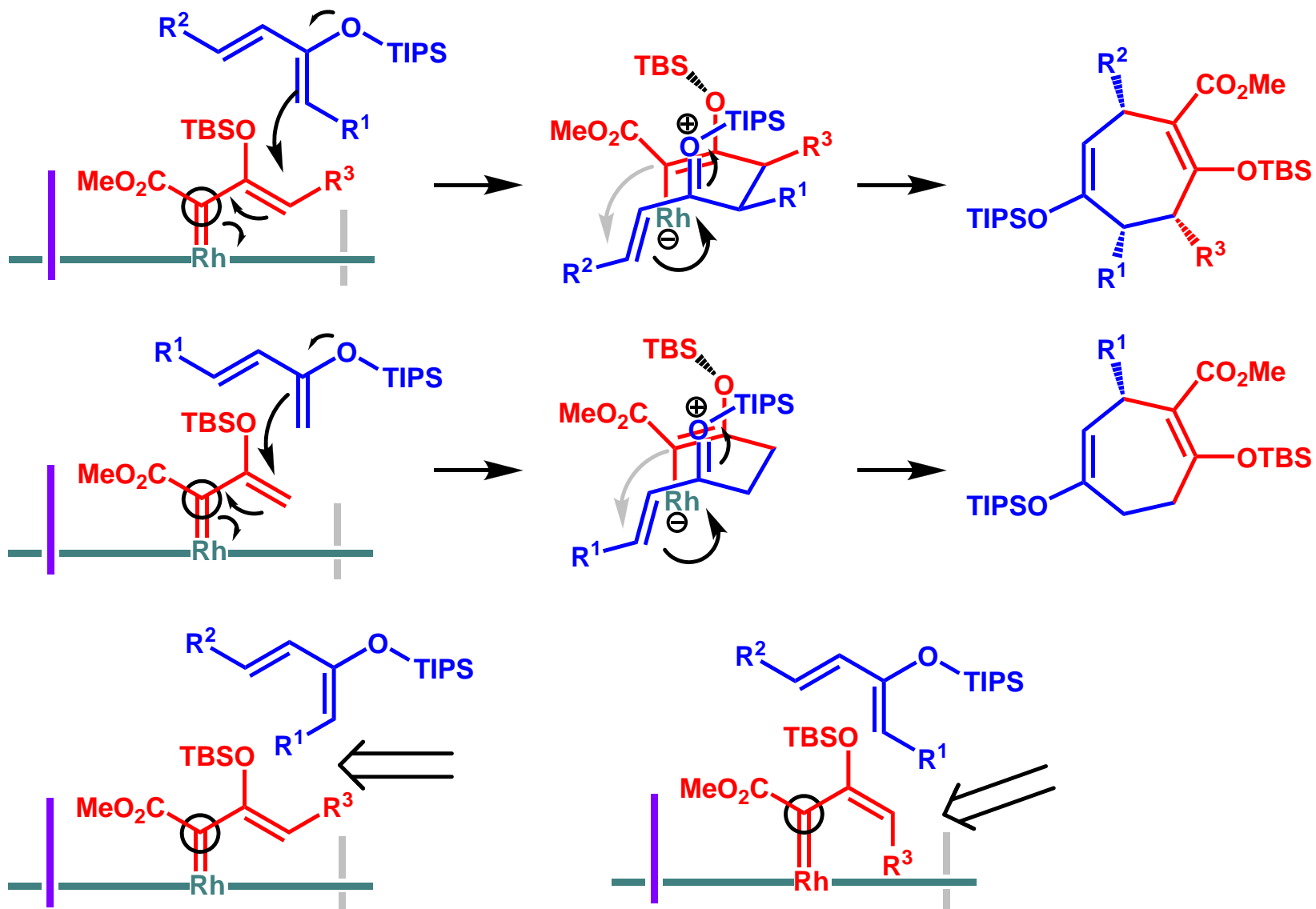
52% yield, 99% ee  
dr > 30:1

# Asymmetric reactions of vinylcarbenoids

---



# Asymmetric reactions of vinylcarbenoids



Cycloaddition reactions play a pivotal role in the synthetic design of complex natural products. **The venerable Diels–Alder reaction is a notable example of the synthetic utility of cycloaddition strategies.** Excellent stereocontrol is routinely achieved, and with appropriate electronic bias in the diene and dienophile, high levels of regioselectivity are also obtained to form the cyclohexene 3. **The defined regiocontrol is a great advantage for the predictable use of the Diels–Alder reaction but it also presents a limitation as the reverse regioisomer 4 is not readily accessed.** Limited methods have been developed to address this longstanding problem but they involve multistep synthetic sequences. **Relatedly, our laboratory has developed a rhodium-catalyzed formal [4+3] cycloaddition between vinyl diazoacetates and dienes.** This reaction is also highly regioselective, as illustrated by the reaction of 1 with the rhodium vinylcarbene intermediate 5 to generate the cycloheptadiene 6, because it proceeds by a tandem cyclopropanation/Cope rearrangement (CPCR). **Herein we describe an alternative and mechanistically distinct [4+3] cycloaddition caused by initial attack of the diene at the vinylogous position of the vinylcarbene instead of at the carbene center.** In this way, we achieve a regiochemical switch of the [4+3] cycloaddition, thus leading to the formation of the cycloheptadiene 7.



In summary, an asymmetric [4+3] cycloaddition between rhodium vinylcarbenes and dienes has been developed. The reaction proceeds with the opposite regiochemistry to the traditional tandem cyclopropanation/Cope rearrangement. An efficient asymmetric cycloaddition was achieved when  $[\text{Rh}_2(\text{S-BTPCP})_4]$  was used as catalyst in hydrocarbon solvents. By an appropriate choice of diene and vinyl diazoacetate, cycloheptadienes with up to three new stereogenic centers can be generated with excellent stereocontrol.