

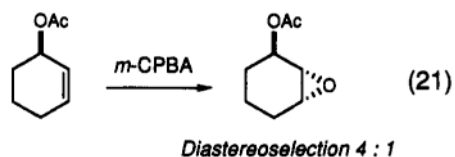
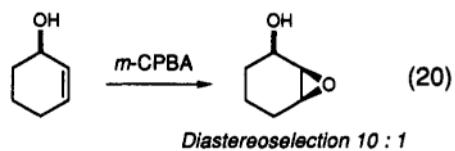
CHEM 6352

Directed Epoxidations

All Figures and Schemes from Hoveda, Evans, Fu *Chem. Rev.* **1993**, 93(4), 1307

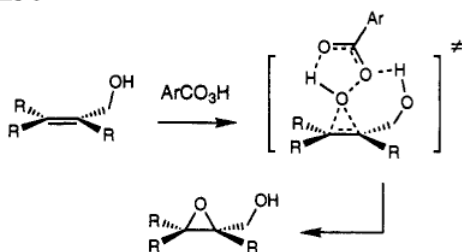
Cyclic Cases with Peroxy Acids

Directed vs. Steric Control



Henbest Model:

Scheme 9



Sharpless Model:

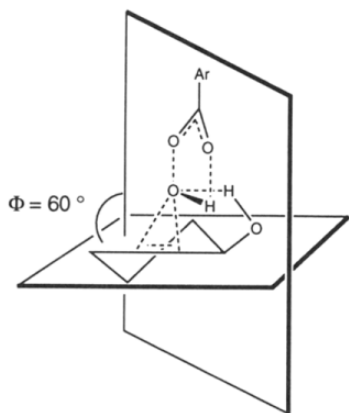


Figure 2. Transition structure for the peracid epoxidation of cyclic alcohols.

Scheme 10

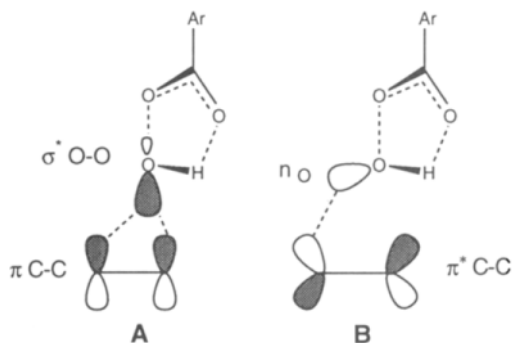


Table 8. Stereoselective Epoxidation of Cyclic Allylic Alcohols^a

Entry	Substrate	Major Product	Selectivity
1			> 20 : 1
2			24 : 1
3			5 : 1
4			*highly selective*
5			*highly selective*
6			*highly selective*

^a Conditions: Perbenzoic acid, perlauric acid, or *m*-chlorobenzoic acid in benzene.

*m*CPBA vs. F₃CCO₃H

Table 9. Stereoselective Epoxidation of Cyclic Allylic Alcohols with CF₃CO₃H

Entry	Substrate	Syn : Anti (<i>m</i> -CPBA)	Syn : Anti (CF ₃ CO ₃ H)
1		24 : 1	50 : 1
2		24 : 1	100 : 1
3		5 : 1	100 : 1

Table 10. Stereoselective Epoxidation of Silyl Ethers with $\text{CF}_3\text{CO}_3\text{H}$

Entry	Substrate	Syn : Anti (<i>m</i> -CPBA)	Syn : Anti ($\text{CF}_3\text{CO}_3\text{H}$)
1		1 : 7	5 : 1
2		1 : 8	12 : 1
3		1 : 4	1 : 6

Table 11. Epoxidation of Cyclic Olefins with Amide-, Urea-, and Urethane-Directing Groups^a

Entry	Substrate	Major Product	Selectivity
1			"highly selective"
2			"highly selective"
3			a. R = NHCONHAc 2 : 1 "highly selective" b. R = NHCONH ₂ "highly selective" c. R = NHCOMe
4			>20 : 1
5			a. R = NH ₂ 3 : 1 b. R = NHBn 5 : 1 c. R = NMe ₂ 10 : 1
6			a. R = OCONHBn >20 : 1 b. R = OCONMe ₂ >20 : 1
7			a. R = CONH ₂ 6 : 1 b. R = CONHBn >10 : 1 c. R = CONMe ₂ 2 : 1

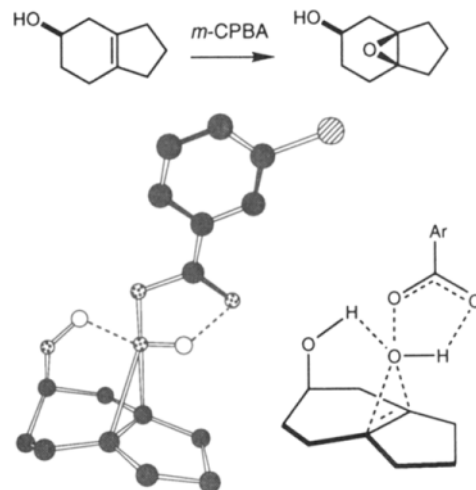
^a Conditions: Perbenzoic acid or *m*-chlorobenzoic acid in benzene.

Table 14. Epoxidation of Cyclic Homoallylic Alcohols^a

Entry	Substrate	Major Product	Selectivity
1			9 : 1
2			"highly selective"
3			16 : 1
4			1 : 1
5			21 : 1
6			5 : 1

^a Conditions: Perbenzoic acid, or *m*-chloroperbenzoic acid in benzene or cyclopentane.

Scheme 11



Cyclic Cases with Metal Catalysis

Scheme 16

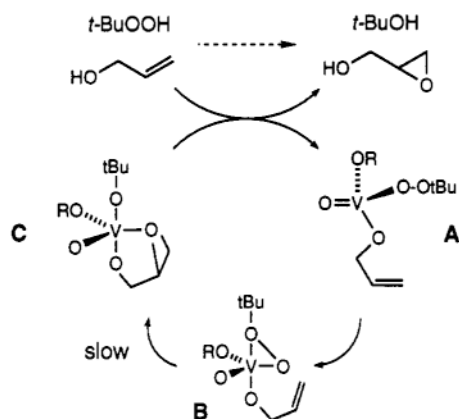


Table 18. Percent Syn Isomer in the Epoxidation of Cyclic Allylic Alcohols

n	VO(acac) ₂	MoO ₂ (acac) ₂	m-CPBA
5	99.2	--	84
6	99.7	98	95
7	99.6	95	61
8	97	42	0.2
9	91	3	0.2

V Epoxidation Needs Pseudoaxial OH:

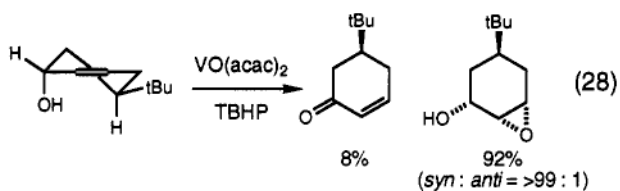
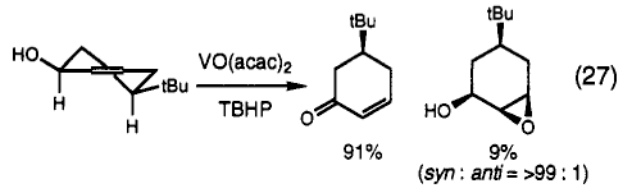
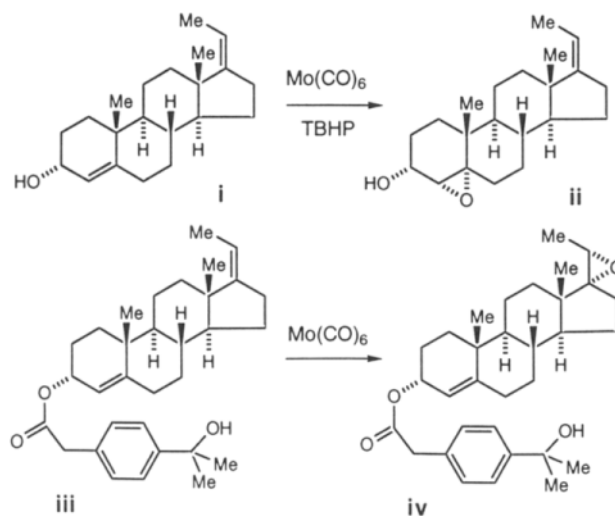


Table 19. Mo-Catalyzed Epoxidation of Cyclic Olefinic Alcohols

Entry	Substrate	Product	Yield (%)
1			78
2			94
3			90
4			87
5 ^a			95
6			--

^a Catalyst: Mo(CO)₆.

Scheme 17



Acyclic Cases: Allylic Alcohols

Scheme 18

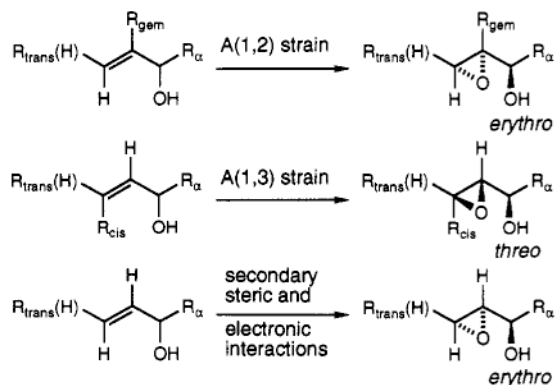


Table 21. Epoxidation Selectivity of Allylic Alcohols

Entry	Substrate	VO(acac) ₂	Mo(CO) ₆	m-CPBA
1		4 : 1	1 : 1	1 : 1.5
2		19 : 1	5 : 1	1 : 1
3		2.5 : 1	1 : 1.5	1 : 1.7
4		1 : 2.4	1 : 5	1 : 19
5		1 : 5	1 : 19	1 : 19

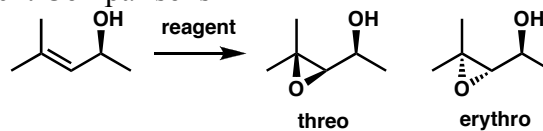
Table 22. Erythro-Selective Epoxidation of Allylic Alcohols

Substrate	Entry	R	Erythro:Threo
	1	Me	4 : 1
	2	<i>i</i> -Pr	5.6 : 1
	3	Me	19 : 1
	4	Bu	49 : 1
	5	Me	2.4 : 1
	6	<i>t</i> -Bu	3.7 : 1
	7		>99 : 1

Table 24. Threo-Selective Epoxidation of Allylic Alcohols

Substrate	Entry	R	Threo : Erythro
	1	Me	3 : 1
	2	SiMe ₃	24 : 1
	3		>99 : 1
	4		6 : 1

Reagent Comparisons

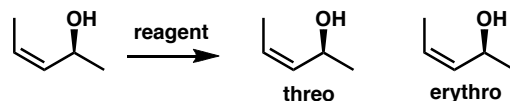


Oshima et. al.
TL 1980, 21, 1657 & 4843

Sharpless et. al.
TL 1979, 20, 4733

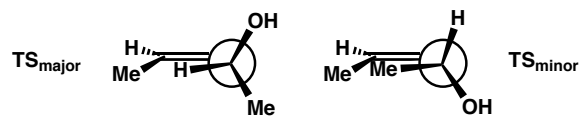
reagent	ratio
mCPBA	95:15
<i>t</i> -BuOOH/VO(acac) ₂	86:14
<i>t</i> -BuOOH/Mo(CO) ₆	95:5
<i>t</i> -BuOOH/(<i>t</i> -BuO) ₃ Al	100:0

Calculated Geometries



ϕ Estimate	reagent	ratio
$\sim 120^\circ$	mCPBA	95:5
40-50°	<i>t</i> -BuOOH/VO(acac) ₂	71:29
	<i>t</i> -BuOOH/Mo(CO) ₆	84:16

$\phi \sim 120^\circ$ for RCO₃H Transition States



$\phi \sim 45^\circ$ for RCO₃H Transition States



Acyclic Cases: Homoallylic Alcohols

Transition State for Homoallylic Vanadium Epox.

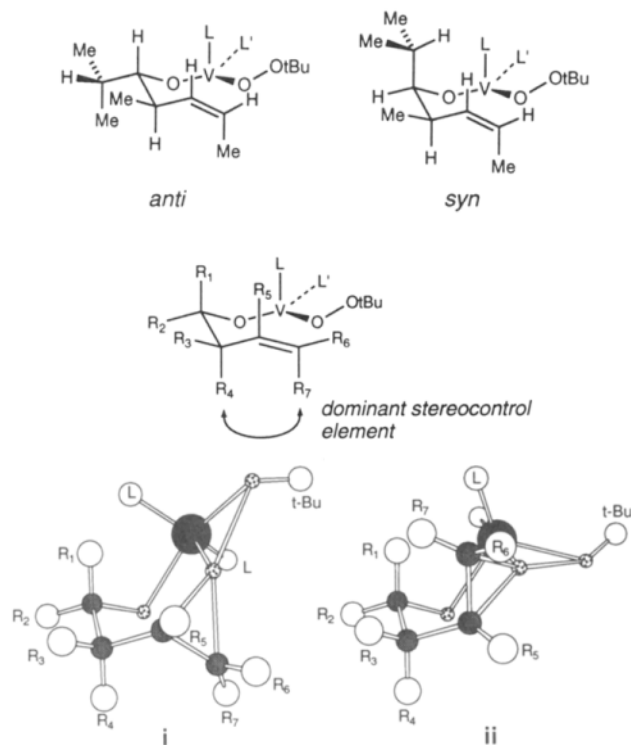


Figure 6. Transition structure for metal-catalyzed homoallylic alcohol epoxidation.

Table 26. Epoxidation of Cis Homoallylic Alcohols^a

Entry	Substrate	Product	Selectivity
1			>400 : 1
2			12 : 1
3			a. R = Me b. R = CH(CH ₃) ₂ 104 : 1 >400 : 1
4			a. R = Me b. R = CH(CH ₃) ₂ 70 : 1 2.1 : 1

^a Conditions: TBHP, VO(acac)₂.

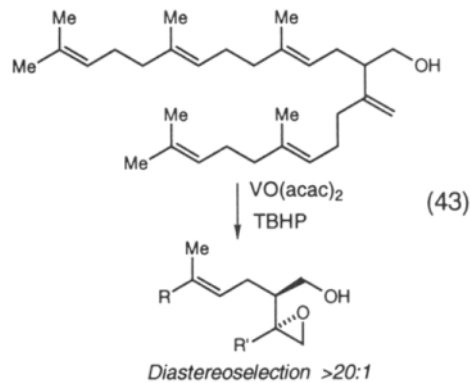


Table 27. Epoxidation of Homoallylic Alcohols^a

Entry	Substrate	Product	Selectivity
1			2 : 1
2			4.6 : 1
3			1.4 : 1 R = (CH ₂) ₇ CO ₂ Me
4			"only"
5			1.5 : 1
6			8 : 1
7			>99 : 1
8			2 : 1

^a Conditions: TBHP, VO(acac)₂.

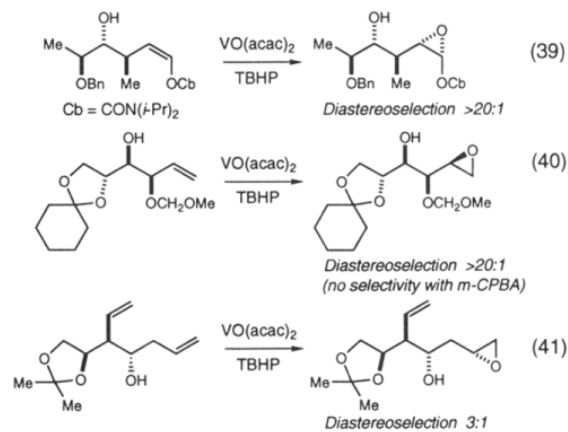


Table 25. Epoxidation Diastereocontrol by Other Stereocenters

Entry	Substrate	Product	Reagent	Selectivity
1			VO(OEt) ₃	5 : 1
2			VO(OEt) ₃	1 : 3.5
3			Ti(O ⁱ -Pr) ₄ VO(acac) ₂ <i>m</i> -CPBA	10 : 1 1.5 : 1 1 : 99
4			Ti(O ⁱ -Pr) ₄ VO(acac) ₂ <i>m</i> -CPBA	2.3 : 1 2.5 : 1 >25 : 1
5			Ti(O ⁱ -Pr) ₄	5.7 : 1